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TECHNOLOGY REVIEW

APRIL 2001

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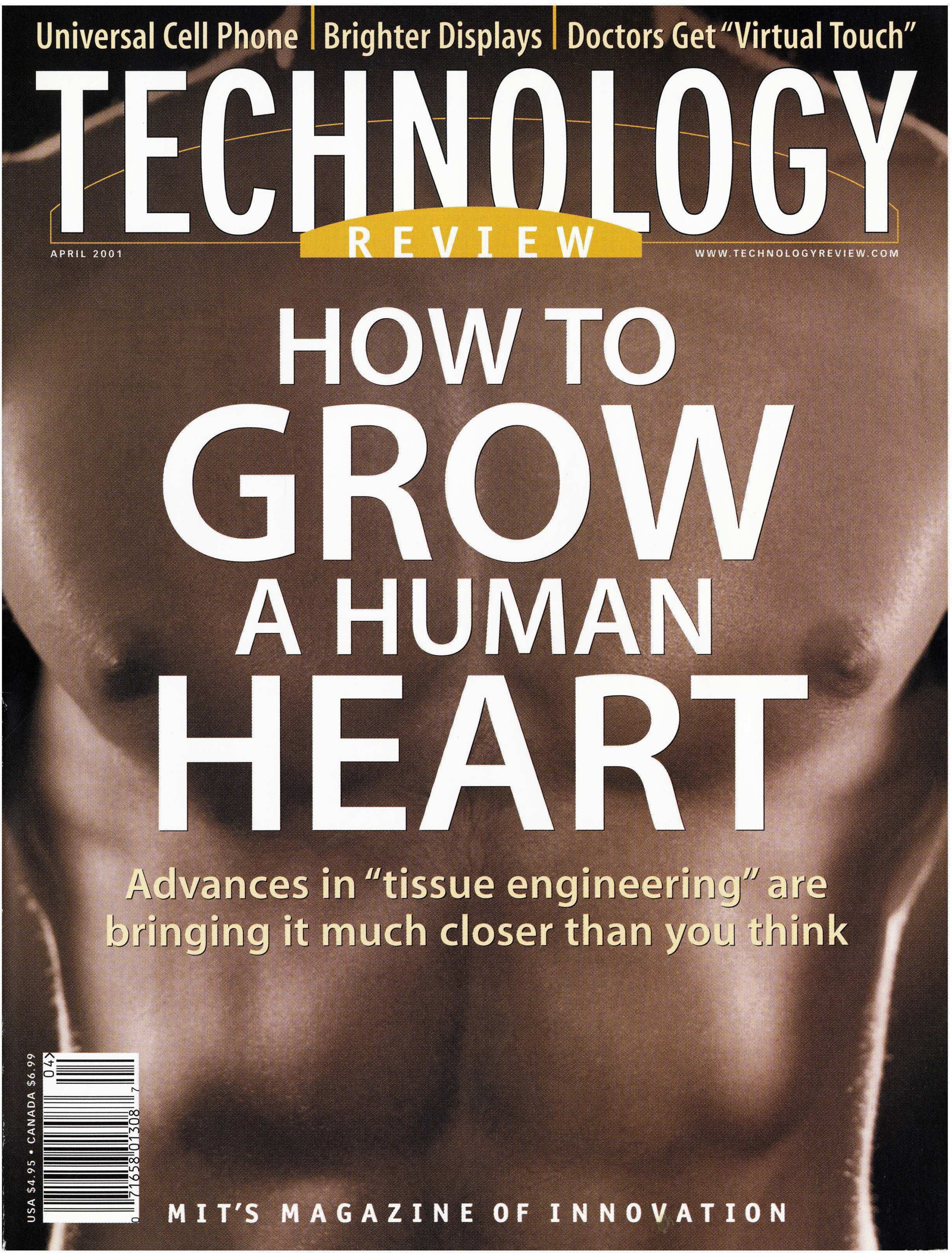

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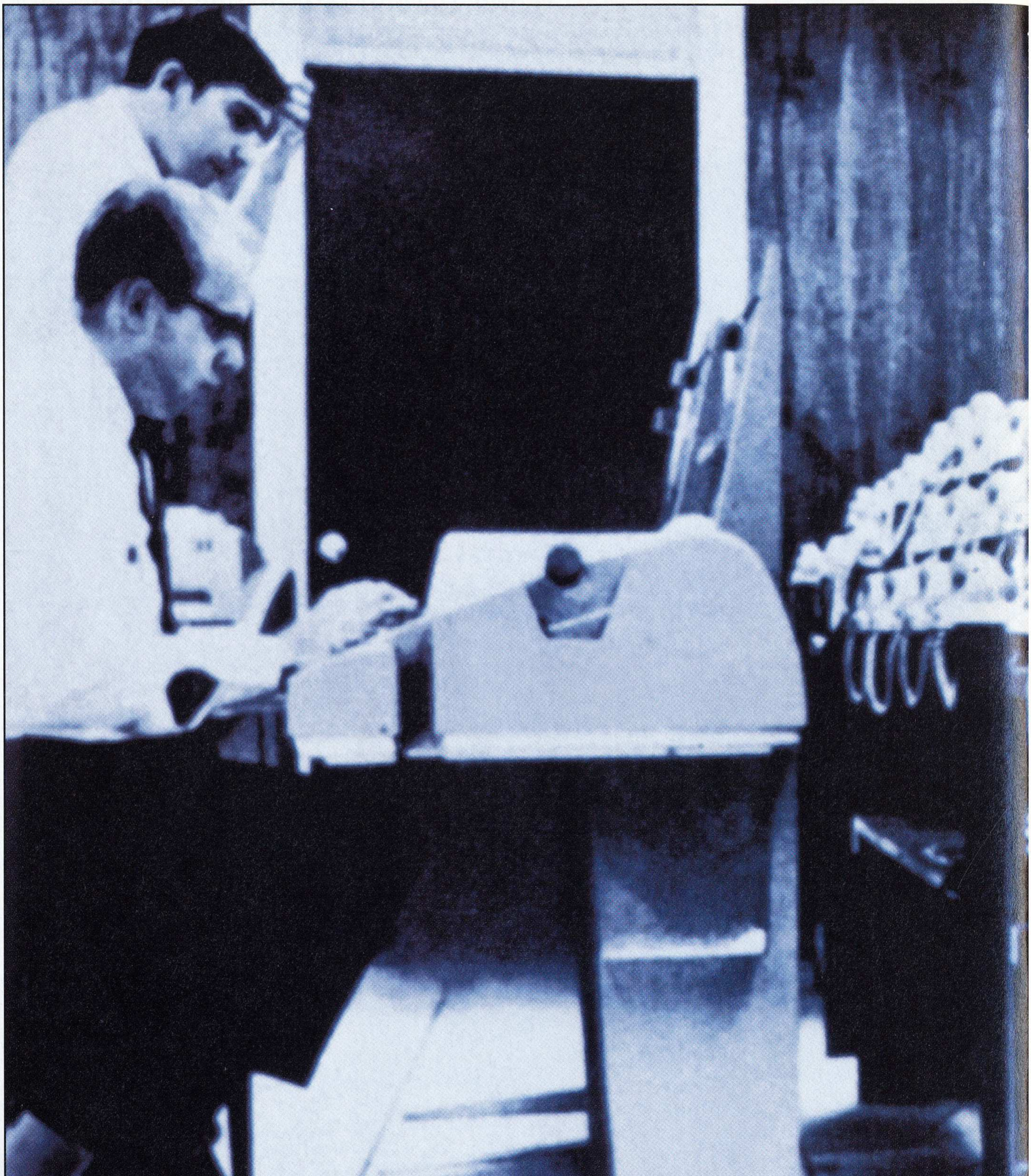

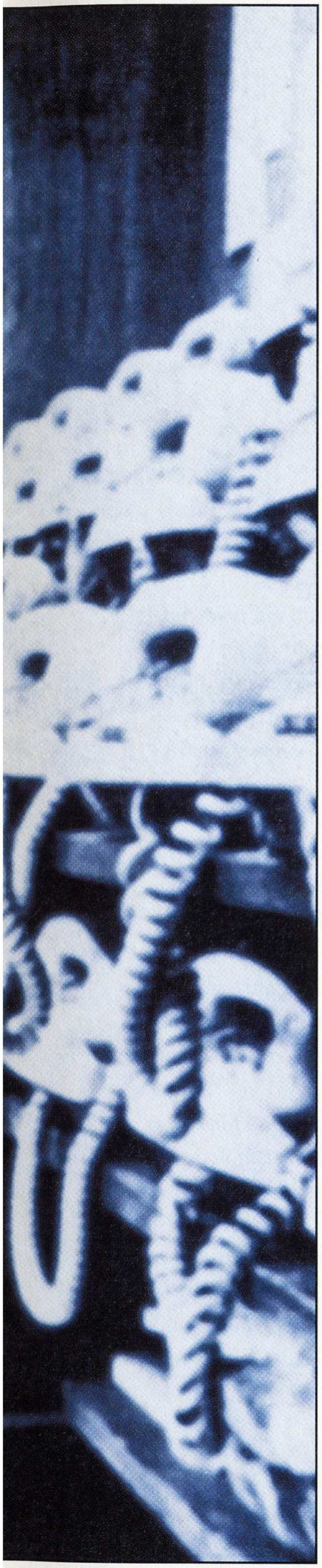

In 1969, we worked on a SECRET GOVERNMENT PROJECT *that became the Internet.*

OHHH, SO THAT'S WHY NOBODY KNOWS WHO WE ARE!

Back in the '60s a small band of computer whizzes was hired by the Department of Defense to work on the ARPAnet. Or what is commonly known as the forerunner to the Internet. These visionaries came from the legendary research and development company, BBN.

Government work being what it is, there wasn't a lot of publicity about this.

Their work did, however, yield many firsts. The first router. The first e-mail message. The first network packet encryption technology and more.

Years later GTE acquired BBN and invested billions to expand their existing infrastructure into a 17,500-mile, Tier 1, fiber-optic global network.

Spun off from GTE last year, this powerhouse of Internet services is known today as Genuity.™ With Data Centers strategically located around the world and Network Operations Centers continually monitoring security and bandwidth for serious eBusinesses everywhere.

Innovation is in our blood. It is at the core of everything we do: Web Hosting, Internet Access, Transport and Security. And now we've combined our expertise in these four areas into an integrated eBusiness Network Platform called Black Rocket.™ The managed eBusiness solution from a single accountable source.

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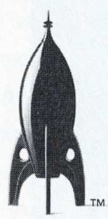

Black Rocket™ is Genuity's eBusiness Network Platform.

A BRIEF HISTORY

BBN

In 1969, BBN was hired by the U.S. government to develop the ARPAnet, the forerunner of the Internet.

GTE INTERNETWORKING

In 1997, BBN was acquired by GTE, the company that created our high-speed, 17,500-mile, Tier 1, fiber-optic network.

GENUITY™

In 2000, GTE Internetworking became an independent company, renaming itself Genuity. Today, Genuity offers a vast array of managed Internet services, including Black Rocket.™

GENUITY™

"Linux is so totally dreamy!"

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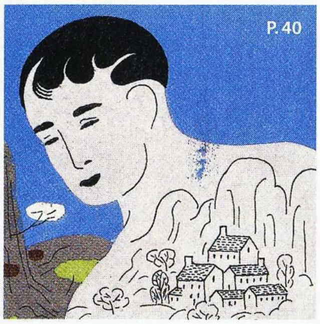

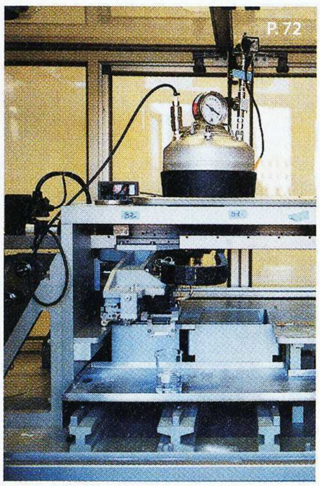

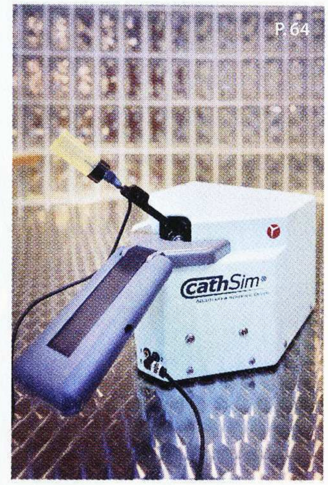

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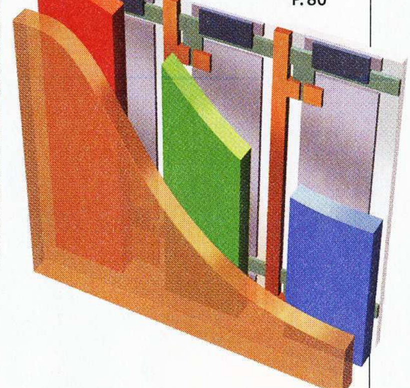

FEATURES

COVER PHOTOGRAPH BY VCL/MIKE OWEN/FPG

AN AT&T BUSINESS IP SOLUTION

VIRTUAL PRIVATE NETWORKS: When MasterCard launched the payment industry's first Virtual Private Network (VPN) three years ago, it turned to AT&T for an IP VPN with bandwidth on demand. The flexible system now operates in 61 countries, allowing MasterCard members to expand network capacity during peak-season loads. No matter what size your business, when transactions soar, AT&T keeps them moving right along.

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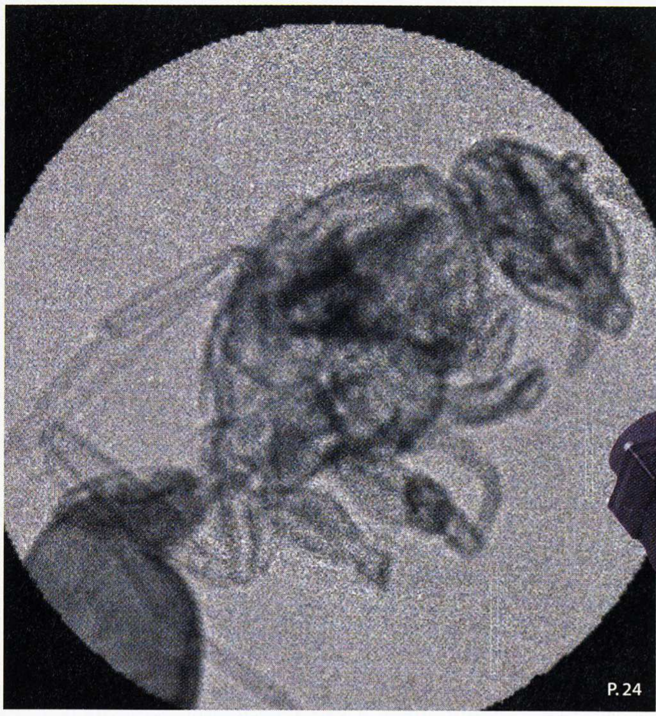

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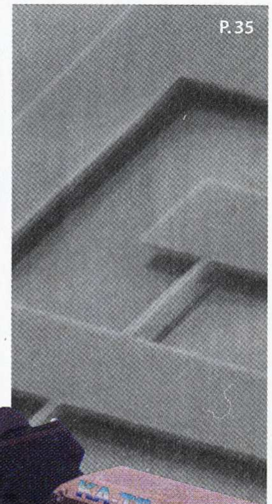

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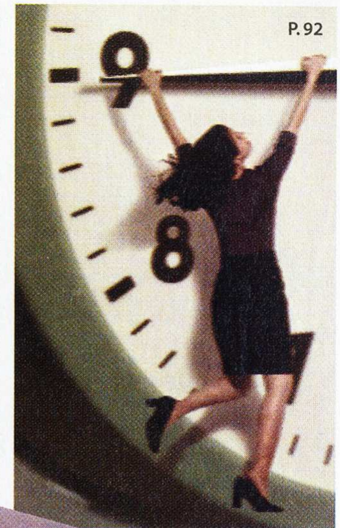

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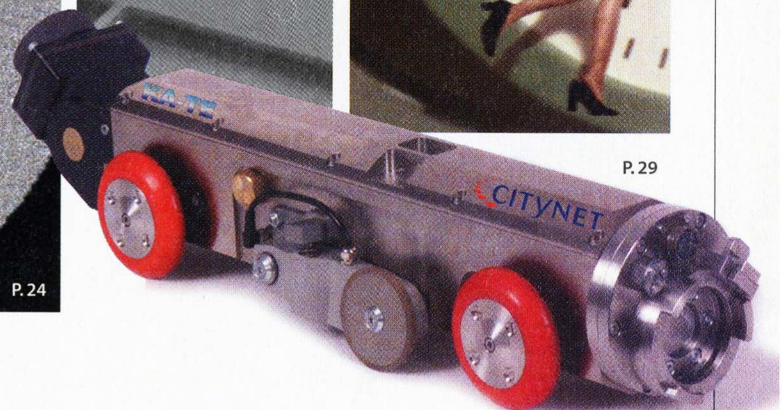

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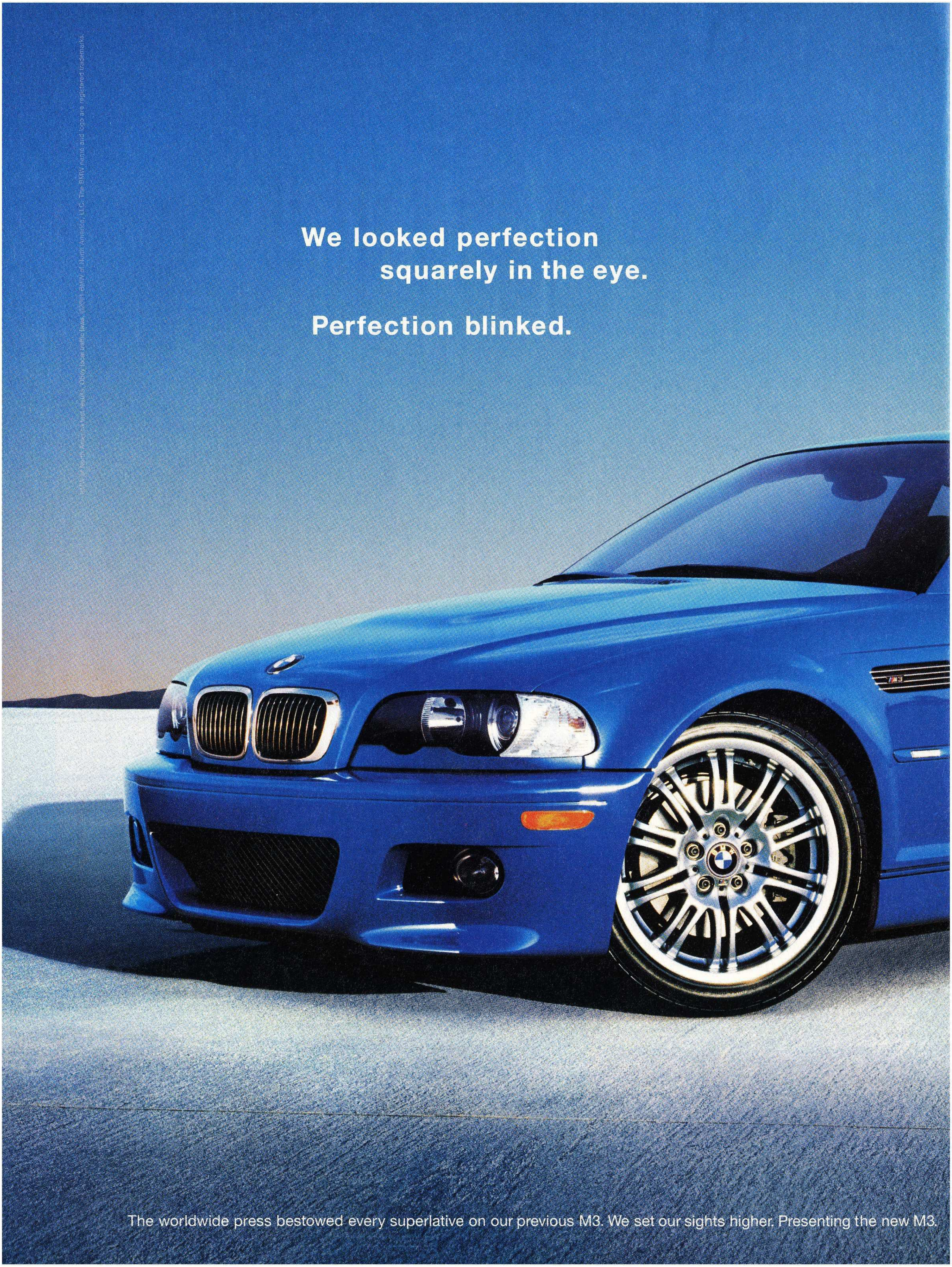

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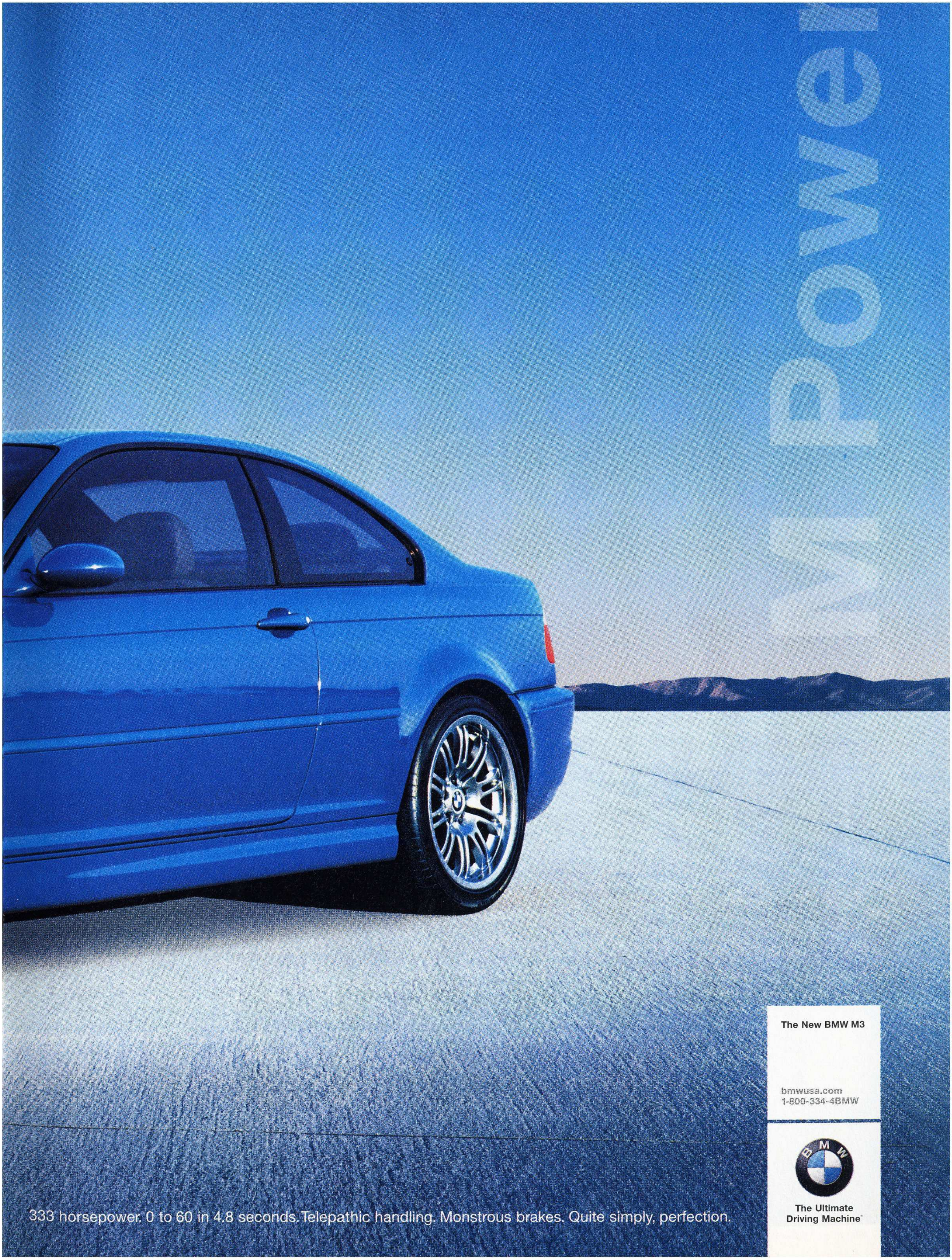
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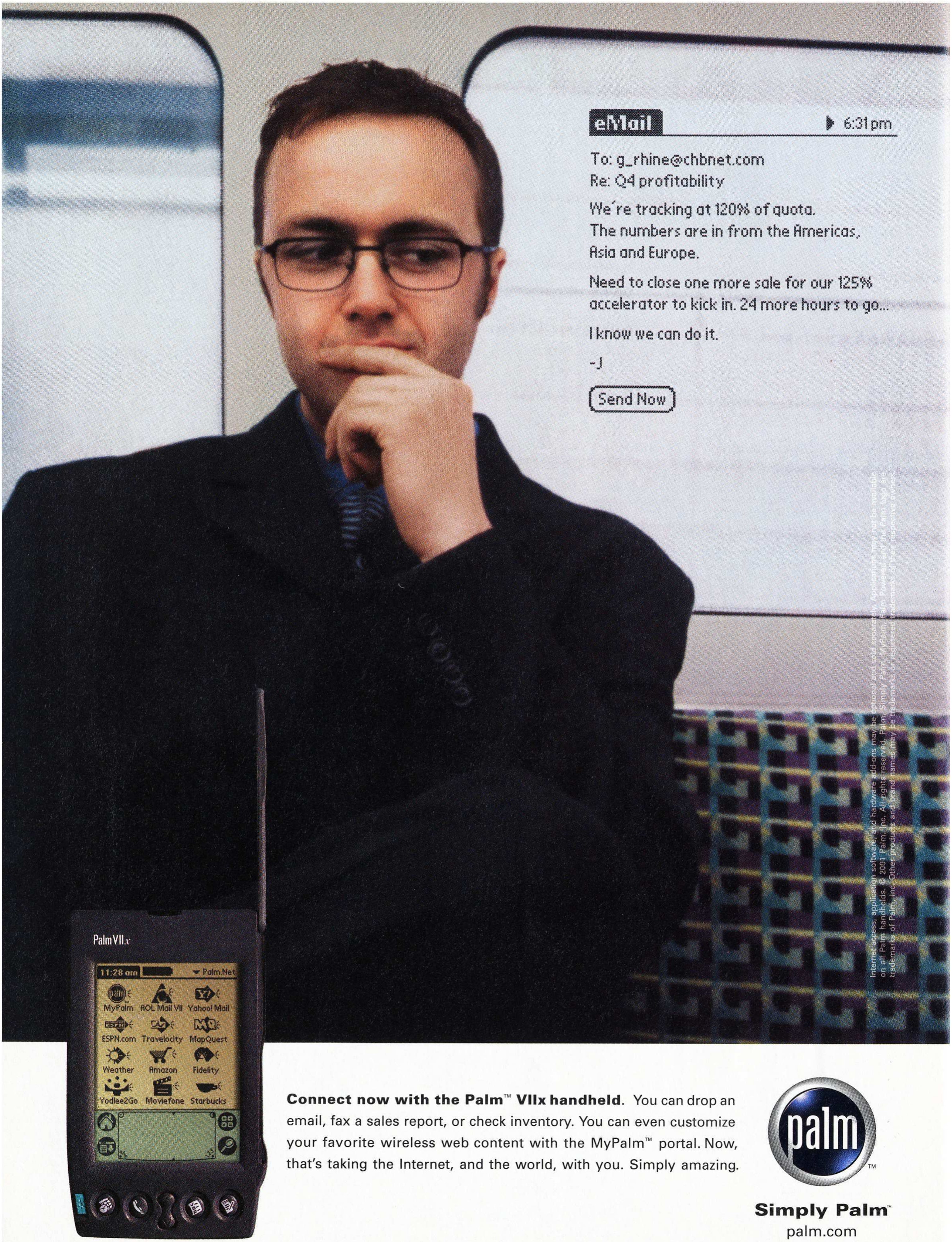

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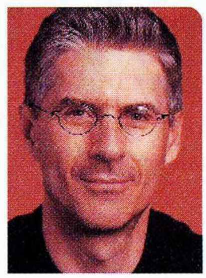
Web Press

YOU MIGHT THINK THAT AFTER BLASTING THE NEW ECONOMY in my last column I'd be abashed to promote a Web site.

Not at all. *Technology Review* accepts the emergence of the Web as a significant new technology. The Web will ultimately have a large impact on how we do business, exchange personal information, and even on how we make art, since almost every new information technology ultimately breeds its own art forms.

In fact, every enterprise that exists to promulgate information must keep up with the Web as it develops. And *Technology Review* is an old hand at the Web business. Our magazine was one of the very first to create its own Web site, in 1994—a project led by two people who have since risen to senior levels in our organization: vice president and general manager Martha Connors, and deputy editor Herb Brody.



Since building that first site (quite primitive by today's standards!), we have maintained a small but efficient Net presence. We have gradually increased the amount of the magazine's content we post and added interactive features, such as discussion forums linked to articles. We didn't have the resources to do more, since we were relaunching our magazine over the same period; the site was maintained by the print staff.

Now all that has changed. We have hired a group devoted solely to extending *Technology Review*'s Web presence. The captains of technologyreview.com are vice president and general manager Bradley Hecht and editor Eric Bender. In a few short, intense weeks, Brad, Eric and their group assembled an entirely new site. There is a completely new design that's cleaner, clearer and crisper. Within the framework of that design, you will still find a healthy proportion of the content of the printed magazine. In addition, we are now, for the first time, offering additional material on the Web that doesn't come from our printed pages. Some of these articles are culled by Eric and his staff from other publications. Some are original pieces written by our Web team. All of this content is available (at least for the time being) without charge.

For convenience and ease of navigation, we have divided this material into three "channels" corresponding to the core areas covered by *Technology Review*: information technology, biotechnology and nanotechnology (into this third channel we've lumped, for now, everything that doesn't fit comfortably into the other two, such as energy and transportation).

The additional content is in principle much like the content of a magazine, but we've also added some features that can't be duplicated in print. Interactive elements of the site, including the discussion forums, have been moved front and center—starting with a forum soliciting your feedback on the new site. The new site makes it easier to subscribe or renew your subscription online. And soon we plan to offer other Web-based services, such as listings of hot jobs in the high-technology sector.

Over the coming months, technologyreview.com will continue to develop, adding new features when they're ready. This evolution will demonstrate the same restraint (no New Economy hysteria here) and high quality that have characterized our work on the Web and in print thus far. Our goal is to broaden and deepen the *Technology Review* community and improve our efforts to help you understand emerging technologies and their impact. After all, that's our mission.

—John Benditt

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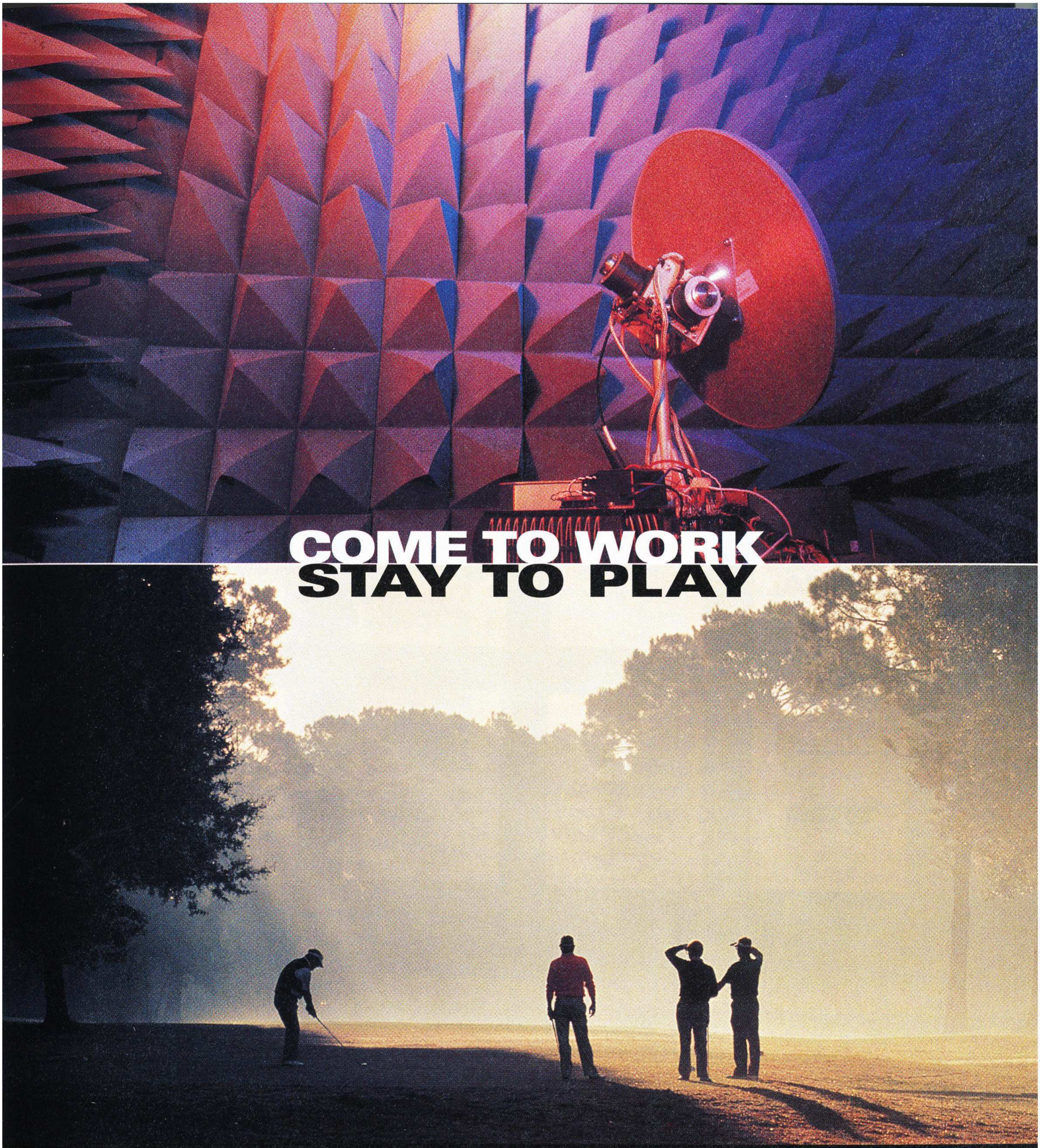
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FEEDBACK *Letters from Our Readers*

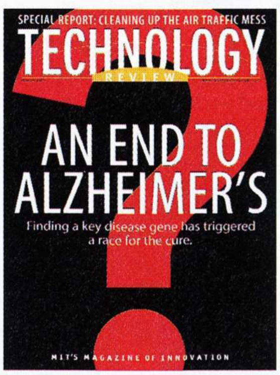
> *"You can make a plane with two buttons, one for up and one for down, and there will always be someone who presses the wrong button."*

Electronic Tagging

A FRIEND POINTED ME TO YOUR ARTIcle "Beyond the Bar Code" (*TR* March 2001), which talks about the future of electronic tags on products.

The article was excellent but barely touched on one of the most exciting potential features of this technology: the ability to give consumers more power over purchasing decisions at the point of sale. Imagine consumers being able to preprogram preferences in their PDAs, such as, seek out products that are recyclable and have recycled content; seek out kosher products; or avoid products with certain features or chemicals, or made by certain companies with bad labor practices, or made in (or even shipped through) certain countries with bad human rights records, etc. An item's electronic tag could easily provide a link to a Web page or online database with all this information. Once companies are able to track such information about every single item they sell, consumers are going to demand access to it as well.

CHRIS STRUBLE
Hewlett-Packard
Boise, ID



Hot, Clean Air

I AM ASTONISHED THAT THE AUTO industry appears to be overlooking the development of high-energy batteries, e.g., the zinc-air and aluminum-zinc batteries that can power electric vehicles with the performance and range of today's gasoline-fueled automobiles.

In "Fuel Cells: A Lot of Hot Air?" (*TR* March 2001), Jules Crittenden notes that the auto industry is forging ahead with the development of a "low-emission" (hydrocarbon/hydrogen) version of the fuel cell to power electric vehicles in the near future. A zero-emission hydrogen fuel cell will not likely be in use until after the year 2020.

A company called Electric Fuel is demonstrating use of the zinc-air battery to power a 40-seat electric bus in a project cosponsored by the Federal Transportation Administration and a smaller electric cargo van in a project cosponsored by the German government.

We could be driving zero-emission battery-powered vehicles within a year or two. Why, then, is the auto industry willing to procrastinate for 20 more years before introducing a zero-emission hydrogen-powered fuel cell?

BILL KING
Houston, TX

JULES CRITTENDEN TALKS of fuel efficiencies and environmental friendliness as if they were the only assets of the fuel cells. But an ability to operate on fuel other than that which is processed from crude oil is more likely to become a prime asset and main driving force in the near future. The fact that these cells can run on hydrogen, methane, natural gas and even carbon monoxide may provide one of the few alternatives the United States will have for countering the stranglehold the world's demand for oil and the oil cartels' prices are placing on us.

I believe that the price of oil will skyrocket in the not too distant future because of increased demand by China and other nations that are industrializing throughout the world. The inability of dwindling oil supplies to keep up with world demand and the greed of the cartels are going to challenge our nation's lifestyle, or existence as we know it.

The scramble to continue our lifestyle will propel the advancement of fuel cells and other means of alternative fuels to the forefront of our priorities. With the price of an alternative fuel no longer a hindrance and the public demanding a solution to diminished living standards, our nation's scientists and engineers will quickly rise to the challenges of the development, production and distribution problems cited for these cells.

WILLIAM D. PATTERSON
Pacific, MO

HYDROGEN IS NOT THAT FAR AWAY unless the oil and gas lobby keep it off the market! With nuclear power you can produce hydrogen cheaper than the current "competition" and in the process kill two birds with one stone: global warming and a power or energy shortage. The reforming of hydrocarbons for fuel-cell use is an interim step, we hope, but the public may reject all hope of ever having a clean environment simply because they like 400-HP diesel or gasoline engines in cars! And by 2025 it may be a moot point.

WILLIAM D. MONTJOYE
San Antonio, TX

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E-mail: letters@technologyreview.com.
Please include your address, telephone number and e-mail address.
Letters may be edited for clarity and length.

Easy Flying?

I THOROUGHLY ENJOYED READING "Flying Made Easy" (*TR* March 2001). It looked like an article from a 50-year-old *Mechanics Illustrated* magazine. The only thing missing was some enthusiastic assurance that the thing could be built for $100 with parts you can find around the house and garage!

Assuming that the problems of air traffic control could be solved—a big assumption at the very least—the inherent dangers and imminent harm that would present themselves upon the slightest malfunction in the vehicle, the guidance system or ground facilities would seem to present significant obstacles to the proliferation of these airplanes. I once had a flight instructor who said that you could make a plane with two buttons, one for up and one for down, and there would always be someone who would press the wrong button.

On the other hand, for someone interested in learning or continuing to fly,

the prospect of a simpler and more error-proof flying system is certainly welcome.

NORMAN A. ABEND
Wayland, MA

Making Splashes

MICHAEL MORITZ'S OPINIONS EXPRESSED in "A Bigger Splash" (*TR* March 2001) surprised me for their insightfulness and maturity coming from Silicon Valley, home of more gunslingers than Dodge City.

His perception of the evolution of most of the new e-tech firms will be 100 percent right 20 years from now when we look back. His prophetic remark that "Every time we tinker with the equation [that meeting customers' needs equals profit] or delude ourselves into believing that tomorrow will be different, we will get into trouble" reminded me of the book by Charles MacKay, *Extraordinary Popular Delusions and the Madness of Crowds*, I read 30 years ago. The introduction was by Bernard Baruch.

A little history will provide perspective for startup companies.

BOB ZILLER
New Richmond, WI

Light-ly Flowing Traffic

AS ONE WHO COMMUTES TWO HOURS each way to a Silicon Valley job, over a freeway system that is nearly worthless, my first thought after reading Simson Garfinkel's column "Internet on a Chip" (*TR* March 2001) was, "Why not assign an IP address to each of the millions of traffic lights in an urban area?" This would allow traffic flow to be synchronized and coordinated so that drivers could go in any direction on major boulevards at a safe speed of, say, 80 kilometers per hour, without having to stop at intersections. Such a solution could free up the interstate highway system for heavy interurban jobs and alleviate the need for continually expanding the expensive freeway network.

VERN KERR
Modesto, CA

Correction

Walt Haas's letter ("Feedback," *TR* March 2001) indicated Idaho as the site of the destruction of the airship *Shenandoah*. The correct site was Ohio.

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STRAIGHT FROM THE LAB: TECHNOLOGY'S FIRST DRAFT

Crack Detective

Under the enormous strain of daily use, the materials used for jet engine turbines and high-pressure bolts can develop fine cracks that lead to disaster. Researchers can identify most of these defects via neutron radiography, a technique similar to x-ray photography; but some cracks are too fine to register. An alternative method, called phase-contrast imaging, can detect even more subtle features, but it requires special equipment running in stringent environmental conditions such as complete isolation from vibration. Recently, however, physicists at the National Institute of Standards and Technology, the University of Melbourne and the University of Missouri, Columbia, have produced high-resolution neutron radiographs using conventional apparatus. The technique works by combining the data from two standard neutron radiographs taken from different angles, then extracting the phase contrast using a computer algorithm. The technique may also be used to study biological tissues: for example, to better visualize tumor boundaries. **—E. Jonietz**

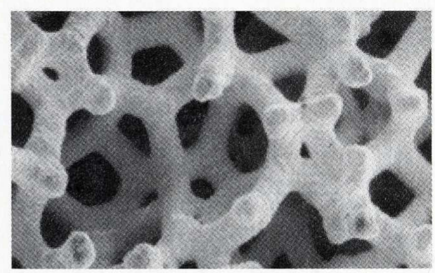
Spherical Robot

Today's robotic arms have limited flexibility, with many robots requiring up to six arms to achieve a complete range of motion. But now engineers at the Johns Hopkins University have laid the groundwork for robots with increased flexibility and accuracy by developing a spherical motor that can turn 360 degrees. Operating more like a shoulder joint than the elbow joints of current design, the prototype comprises 16 electromagnets arranged around a hollow sphere. When activated by a software-controlled electrical signal, the electromagnets attract 80 permanent magnets located inside the sphere, thereby causing motion. Within five years, the motor may be used in omnidirectional wheels, robotic cameras and even a smart computer mouse, directed by software agents. **—V. Herrera**

Predicting the Crash

More and more PC users leave their computers on all the time, but after a few days of usage, the chance of a system crash increases dramatically. This phenomenon—known as "aging"—occurs from a steady accumulation of the small programming errors common in software. There's no cure for aging except to reboot the system, but now researchers at IBM, led by Tom Bradicich, have developed a software rejuvenation program that can predict when a computer is close to the edge and warn users it's time to reboot. The software is built into the latest version of IBM Director, the software that runs on IBM's low-end servers. Bradicich says the program could be modified for use in other Windows and Linux computers. **—E. Brown**

Artificial Thymus



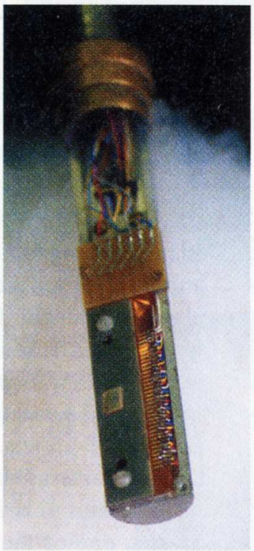
Laboratory production of T cells—immune cells that grow naturally in the thymus gland—could provide new therapies against cancer, autoimmune disorders and organ transplant rejection. But they're hard to grow in culture dishes; current methods yield too few cells of too little variety. Researchers from Massachusetts General Hospital in Boston and the Woburn, MA, biotechnology firm Cell Science Therapeutics have developed an artificial thymus that solves both problems. Constructed from a porous metal-and-carbon material typically used for bone repair and arranged in a three-dimensional matrix, the structure mimics the functions of a living-tissue thymus, generating a bumper crop of T cells that can adjust to new threats. Clinical trials start in 2002, with commercial availability expected a few years later. —M. Wortman

A Clean Start

When you warm up your car, only one in five injected gas molecules actually combusts and delivers power. The rest puddle up and evaporate, resulting in excessive emissions of hydrocarbons. The solution—a special fuel designed to burn efficiently during warmup—was developed years ago, but car manufacturers decided it wasn't practical to expect consumers to keep two tanks filled with different fuels. Now, engineers at the University of Texas and Ford Motor have devised a way to distill the special "warmup" gas from standard gasoline within the engine itself. The system, which could reduce auto emissions by over 50 percent and carcinogenic toxins by 80 percent, should be available within four years. **—E. Brown**

Fast Clocks for Fast Chips

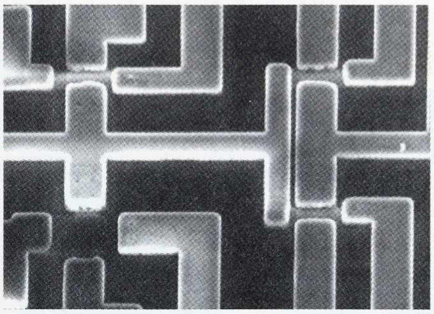
In the world of high-speed computer chips, timing is everything. Without a clock, processors are useless, and the faster and smaller the chip, the harder it is to keep steady time. The latest superconducting chips—circuits that deliver astonishing electrical speed when kept at extremely cold temperatures—are the electronic equivalent of an untamed bucking bronco. In search of a faster timing device that can harness their power, Mark F. Bocko, professor of electrical engineering at the University of Rochester, has developed a clock with a built-in diagnostic chip that can measure and adjust its own timing. Already, Bocko's team has successfully clocked a superconducting circuit running at 50 gigahertz. The clocks could eventually handle chips running at "several hundred gigahertz," says Bocko. The team is working with an Elmsford, NY, electronics company called Hypres to construct superconducting equipment for wireless communications. **—C. Conti**



Superconductor Power

Some of the blackouts that struck California this winter might have been avoided if power companies could more quickly move large amounts of electricity between regions. Such a boost may be possible with a new type of superconducting tape invented at Los Alamos National Laboratory's Superconductivity Technology Center. Made from nickel alloy, the tape is coated with fine layers of zirconia using a pulsed-laser process that precisely orients the zirconia grains after deposition. Then subsequent layers of nickel are applied to create a superconducting film as thin as six micrometers. The tape carries one million amperes per square centimeter of current, about 14 times the capacity of today's bismuth-based superconducting tape and 200 times better than copper wire. The liquid-nitrogen-cooled tape can operate at a relatively balmy -196 °C, making it far more economical than many existing high-capacity tapes that require cooling by liquid helium at temperatures as low as -269 °C. The new process is also much faster than earlier methods. Within two to three years the tape should appear in products including transformers, electric motors and transmission cables. **—V. Herrera**

Quantum Leap



Each year, the size of transistors shrinks, thereby improving performance. Yet transistors must be big enough to allow electrons to pass through. Preparing for an inevitable impasse, Toshiba recently demonstrated a transistor that can turn on and off based on the movement of a single electron. Unlike other experimental quantum-level transistors, the device can operate at room temperature. It's also the first successful hybrid circuit, mixing single-electron transistors with traditional metal-oxide transistors, which are required to boost the weak quantum-level signal. Chips based on the circuit should offer blazing performance and low power consumption. Before building a full-fledged processor, researchers face challenges such as finding a way to protect the chip from the disrupting effects of stray electromagnetic fields, electrical discharges and physical movement. Hybrid chips should be available commercially by 2010.

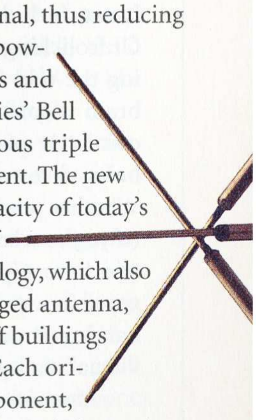
—C. Conti

Magnetic Chip

Computers process data electronically and store data magnetically; but what if you could make a magnetic processor? A microchip made of magnetic semiconductor material would have unique properties; for example, it could store information while simultaneously performing computations. To make a magnetic chip behave like an electronic one, researchers have tried to control the spin of electrons, with clockwise and counterclockwise movements representing the zeroes and ones of a digital system. Previous attempts have required extremely low temperatures, making them costly and impractical, but materials scientists at North Carolina State University recently built a prototype that functions at a range of 38 to 75 °C. The researchers accomplished their goal by "adding manganese to gallium nitride," says electrical engineering professor Salah M. Bedair. The rest of the recipe is a secret while the group's patent is pending. One potential application: a laser or LED that can be tuned to different wavelengths by adjusting a magnetic field. Such a device could be valuable for fiber-optic communications. **—C. Conti**

Wireless Triple Play

One of the biggest obstacles to boosting transmission speed on wireless data networks is the interference caused by buildings. In cities, signals become so scattered that cellular base station antennas often struggle to gather in a complete signal, thus reducing overall performance. Rather than try to overpower the interference problem, Michael Andrews and his team of researchers at Lucent Technologies' Bell Labs decided to embrace it with an ingenious triple antenna that thrives in a chaotic city environment. The new antenna promises to deliver six times the capacity of today's single-antenna networks and triple that of experimental dual-antenna systems. The technology, which also requires that cell phones include a three-pronged antenna, exploits the fact that radio signals bouncing off buildings arrive at a receiver in different orientations. Each orientation has an electrical and magnetic component, and each of these could be made to carry different information. Wireless equipment vendors are now evaluating the technology for potential use in commercial products. **—E. Brown**



Wired Kingdom

Last year, more than 134 million people visited zoos and aquariums in the United States—more than attended all major sporting events combined. Even more telling, nearly 60 percent of households include dogs or cats; more than fifty percent of pets receive holiday presents, and one-quarter of pet dogs sleep in their owners' beds (you know who you are). In fact, 10 percent of dog owners are more attached to their dogs than to their spouses.

Evidence of our aching need for animal companionship doesn't stop there. Look, for example, at trends in high-tech toys. Six million Tamagotchis—small LCDs displaying pseudopods that "eat" and "grow"—were preordered for U.S. sale, after sales of four million in Japan. Sales of the Gremlin-like, voice-mimicking Furby are in the tens of millions. Sony's digital dog, Aibo, costs nearly 10 times as much as a real dog, but 3,000 of them sold out in 20 minutes; 100,000 have been sold since. Tiger sold 10 million Poo-Chi robot dogs last year. Cloning of pets has emerged as a real business. The human yearning to be in touch with animals is very deep indeed.

To gaze into the eyes of an animal, even for an instant, is to experience an awesome connection with another living being, transcending the species gap. It may be hide-and-seek with a puppy. Or frolicking with a dolphin (and having the odd feeling that the dolphin's brain is considerably larger than your own). Or peeking out of a tent and being face to face with a polar bear. Whether playful, inspiring or terrifying (if you're seen as lunch), these encounters have a power that can't be conveyed in words. You have to feel it firsthand: not on a movie screen, not in virtual reality, but in *real* reality.

Most of us don't know what we're missing, of course. Few people have the privilege of visiting locales such as the magical, otherworldly Galapagos Islands. Setting foot there is like visiting a zoo, except *you* are the animal on display. A mockingbird flits over and lands on your head. Take a swim and seals join in. Penguins, who are so comically awkward on land, streak past in the water like little F-15 jets. Visiting the place blew Charles Darwin's mind and inspired him to write *On the Origin of Species,* one of the most momentous books in science.

But it's said that one island in the archipelago is different. There, the birds and seals run away and hide. A visitor, taken aback by such un-Galapagos-like antisocial behavior, asked what was wrong. "A few centuries ago," his guide said, "hunting was done on this island, and only here. The animals learned to fear man—and they never forgot." Perhaps that one island was a lot like the rest of our world.

Just as this article was going to press, a tanker carrying 900,000 liters of diesel oil ran aground by San Cristobal island at the eastern end of the Galapagos (www.galapagos.org) and began leaking. Seals 50 kilometers away turned up with gooey oil in their fur. The extent of the damage is not yet known, but the

LEIGH WELLS

consequences of such a poisonous wreck could be catastrophic in that singular, fragile ecosystem. It may be an extinction event for many species. The Charles Darwin Research Station is now urgently soliciting funds for help online (see www.darwinfoundation.org).

native situations. You can even steer the camera to get a better view. In addition to letting us peek at exotic wildlife, his system has the bonus effect of making it harder for poachers to do damage: thousands of people who care are always keeping an eye on things.

pooch's reaction through a video link (see www.media.mit.edu/~benres/research.html).

Our pets are truly friends. They have personalities. They play. They mope. They dream. They enrich our relationships and teach us lessons, especially in a world where, too often, humans behave worse than beasts. And animals possess real feelings, too. Is a bird sad when it's singing? Or a kitten when it swats a ball of yarn? A dog when it's gnawing a bone?

As wilderness gets ever more rare, one of the best ways that technology can serve us is in bringing us closer to the wild without destroying it.

Halfway around the world we find another example of a remote ecosystem that offers the most adventurous among us a glimpse of the wild, and that, like the Galapagos, is suffering from human presence. Everyone I know who has encountered the mountain gorillas in the Virunga rain forest on the borders of Rwanda, Uganda and the Congo considers it to be a life-altering experience. Yet vital habitat is being destroyed as sprawling human populations encroach. Amid the regional wars and horrific genocide, gorillas seem of little consequence. The animals are often killed by marauding soldiers and slaughtered for "bushmeat" by poachers. It might as well be cannibalism: about 98 percent of our DNA is the same. Fewer than 650 of these gorillas remain.

As wilderness gets ever more rare, one of the best ways that technology can serve us is in bringing us closer to the wild without destroying it. Recently, new technologies have enabled us to be "with" wild animals in a way never before possible. Cinematographer Daniel Zatz uncovered a useful clue when he was in the field struggling to capture good footage. He just couldn't get close enough to film the wildlife: the animals ran away.

One frustrating morning, he laid his video camera on the riverbank and went to get a sandwich. Upon return, he noticed that bears were strolling around near the camera. Birds were practically perched on it. That told him all he needed to know: the camera wasn't the problem; he was. So he took Webcams a step further with www.seemorewildlife.com. With cameras in delicate places, like elephant-seal breeding grounds or grizzly bear fishing spots, the site lets online viewers watch animals in their

Extending the idea to a greater range of habitat, Greg Marshall of National Geographic Television has spent the last 10 years perfecting the Crittercam, a tiny submersible video camera that can be worn by marine animals. It's a simple idea, not unlike a quarterback's helmetcam in a football broadcast. Suddenly it has become possible to ride on the back of a tiger shark, or dive thousands of feet with sperm whales, seeing the world from their point of view. The first video I saw was of penguins taken *by* penguins in the Antarctic. What a ride!

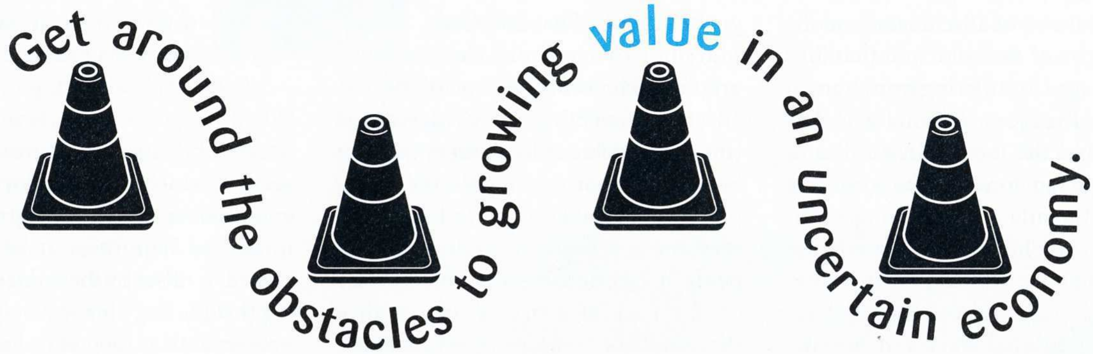
Now if we could just talk with the animals. Actually, research is bringing us a little closer to this Dr. Dolittle fantasy. Irene Pepperberg has been teaching African grey parrots to converse in basic (you might say "pigeon") English. And recently, she and her students at the MIT Media Lab got them online—inventing systems that can potentially enrich the parrots' lives. Their "InterPet Explorer" gives the birds a smart perch, equipped with a kind of joystick and liquid crystal display to access music, watch videos of other parrots or friendly trainers, and potentially make contact with other birds (see www.media.mit.edu/ ~impepper/petprojects/).

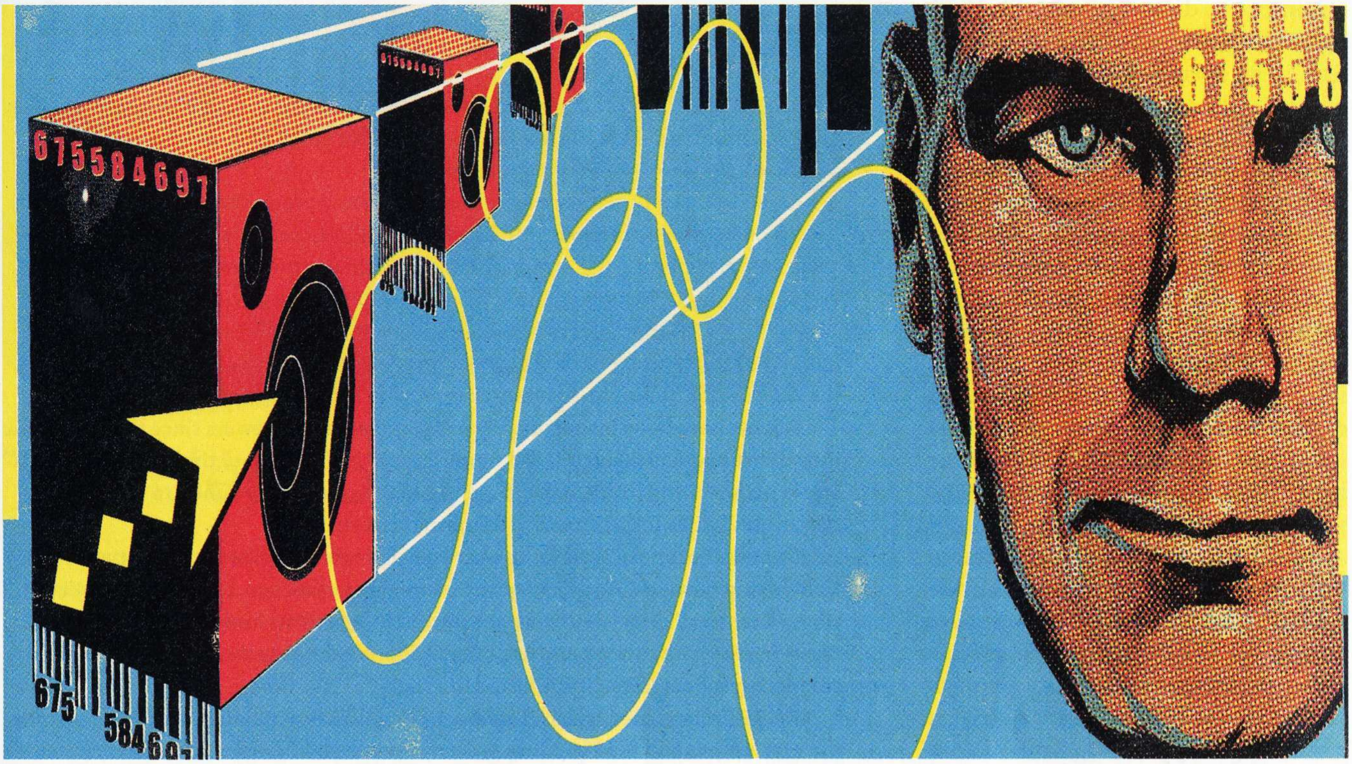
Other developments could bring us closer to animals that are closer to home. Pepperberg's colleagues Bruce Blumberg and Benjamin Resner, for example, have devised a system that allows away-from-home dog owners to play with their pets through the Internet. Using "Rover@Home," the owner can, for instance, remote-control a squeeze toy, dispense treats, and speak to the dog, all the while watching the

One very real feeling is loneliness. When you come home, is your dog just a teensy bit happy to see you? There's a sense in which all of that joyful barking and slobbering, the wagging tail, the unalloyed happiness at being reconnected, is offset by the sadness of knowing that the dog's life will only last about one-seventh as long as its human companion's. My heart broke when our sweet, affectionate malamute, Tasha, passed away with her head in my hands eight months ago. It was not an unexpected event (fortunately, she had lived a long and happy life). But the sadness and sense of loss were more than I'd imagined, and the frustration of being able to look at her and pet her, but not speak to her, was almost unbearable.

Will technology ever produce a linguistic bridge between species? It's still a fantastic question. But whether it does or not, our pet relationships are a powerful motivation to use technology to connect more deeply with the animal world. To ask why it's useful to build interfaces with animals would be like asking Darwin, why go sailing?

But what's extraordinary, especially considering how much we stand to learn from animals, is how we have scarcely begun to evolve technologies to communicate with them. The work by Zatz, Pepperberg and others is helping to show us the way. Let's not forget that "pet" is not just a noun, but also a verb to describe the way you touch someone you love. And being in touch with animal friends, whether technically mediated or not, really matters. ◊


Get around the obstacles to growing value in an uncertain economy.



TAVIS COBURN

The End of Free Music?

New software provides copyright protection for content providers

INTERNET | Start with low-cost recordable storage media—rewritable DVDs and the "flash" memory used in such devices as MP3 players, for example. Add file-compression protocols that make it easy to send music, video and large texts over the Internet. Mix in free software that lets you find and download the files you want from any computer on the Web and copy them to those cheap media. It's a recipe for the end of copyright protection as we know it. What Napster has done to music is just the beginning; movies, books and games are also being reduced to so many zeroes and ones, shot around the world over the Internet and copied at will.

While the march towards a copyrightless society has seemed all but inevitable to some observers, a new technology developed jointly by IBM, Intel, Toshiba and Matsushita Electric could give control back to copyright owners. The technology, known as Content Protection for Recordable Media, or CPRM, allows content producers to specify how many times a consumer can copy a given file. When you buy and download, say, the latest album from Metallica, your MP3 player would use the rights-protection system and the serial number already on your memory card or disk to encrypt the file and create a unique "key" for it. That key lets the music player know whether or not the file is stored on an authorized disk or memory chip. When you want to listen to your album, the player checks for the digital key; if everything matches up, the file is decrypted and your music will begin to play.

The copy-protection system won't work unless it is deployed in the original files, in storage media, and in media players. Hence the need for entertainment companies, makers of storage devices and makers of media players all to license the copy-protection technology and implement the system.

Despite this daunting requirement for cooperation among disparate groups, the technology does solve a problem that some experts claimed was all but unsolvable: how to make a protection scheme that is not only cheap to deploy and easy for customers to use, but virtually hackproof as well. The identification codes used by the copy-protection system have been part of standard storage media for many years. And the number of key combinations they provide is "greater than the number of protons in the universe," according to Jeffrey Lotspiech, research engineer at IBM's Almaden Research Center in San Jose, CA.

Not surprisingly, there are already copy-protection strategies on the market.

Liquid Audio, a private Silicon Valley company, introduced a copy-protection scheme for digital music in 1996. Microsoft provides a digital-rights manager in its operating system, to protect content sold or accessed in Windows Media formats.

Since there is as yet no clear winner among these technologies, record labels, audio and video distribution sites and device makers are likely to support many or all protection schemes for now. Sony, for example, supports both Microsoft and Liquid Audio and is evaluating the new technology developed by IBM and its corporate partners. Meanwhile, IBM has just started installing CPRM in miniature hard disks used in digital cameras and portable digital music players.

Brad Hunt, chief technology officer of the Motion Picture Association of America, says that member companies are negotiating license agreements for the new copy-protection technology, although he would not give a date for when it would begin appearing. And Warner Music Group has already signed on for all of its record labels.

Of course, any technology that prevents unauthorized copying is going to be controversial. "We're extremely concerned that hardware manufacturers seem willing to re-architect our computers, building in restrictions that go far beyond current copyright law," says Robin Gross, staff attorney at the Electronic Frontier Foundation, a group that monitors the electronics industry for threats to personal freedom. "That's trampling on the rights of consumers."

Such logic baffles the corporate developers of CPRM, who argue that without these protections, some copyright holders would simply never make their content available to consumers in new digital formats. "We're not totally nuts," says Donald Leake Jr., program director for IBM's copy protection business development. "We're in a business that depends on consumer trust. These charges that we're invading people's privacy make no sense at all. We just want to make sure that the people who want to buy these products can."

—Claire Tristram

Sewer Bots

They brave the city's bowels to bring you bandwith

ROBOTICS | A small army of robots is infiltrating the sewers in our central cities. Their mission? To deliver the blazing speed of fiber optics without digging up the streets—a slow, costly and unpopular process.

Slinking through sewers may sound like a messy proposition, but it has earned $100 million in venture capital for Silver Spring, MD-based CityNet Telecommunications—the company that hopes to use the sewer robots to wire up cities throughout the United States. "The one clear pathway that gets you down the street and into every building is the water and sewer system," says CityNet's CEO Robert Berger, a former telecommunications lawyer and current vice chairman for the Washington Suburban Sanitary Commission in Maryland.

Robots have been inspecting, cleaning and repairing sewers since the 1970s, but they didn't begin tackling telecommunication's "last mile" until the late 1980s, when Tokyo planners and robot maker Nippon Hume saw an opportunity to string bandwidth under Tokyo's narrow, congested streets.

Sewer robots have since lit up over 900 kilometers of pipes across Japan. Networking firms in Europe joined the game three years ago, but it wasn't until this winter that North American firms got started using robots built by Robotics Cabling of Berlin—which acquired and upgraded Nippon Hume's technology—as well as competing robots from Zürich-based KA-TE.

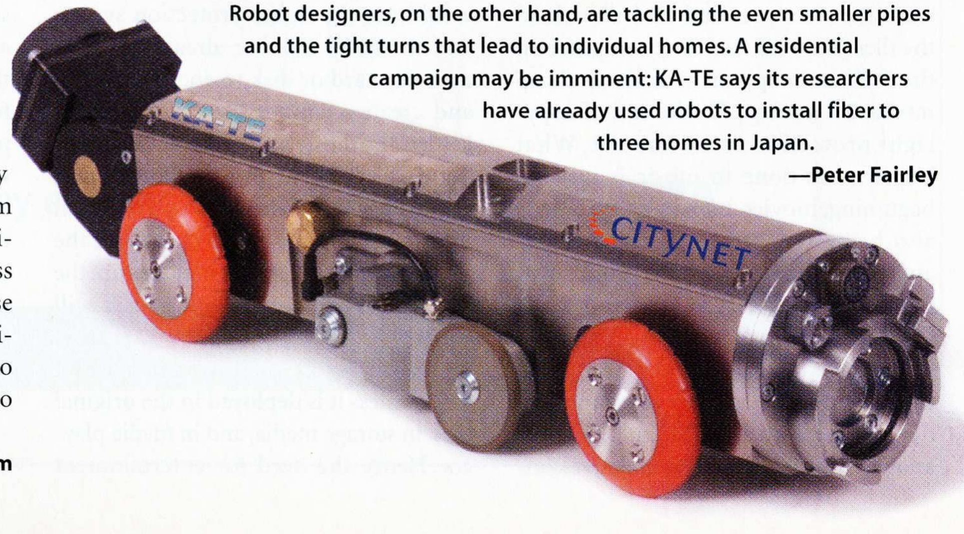
KA-TE's robots prep sewers for fiber optics by fitting stainless-steel bands inside the sewer pipes and then clipping as many as nine stainless-steel conduits to the bands. Conventional cables with 144 fibers can then be blown under pressure into the conduits from street level—either immediately or later on, as neighborhood network demand grows.

In contrast, Robotics Cabling's robots simply finish a job that humans start. Operators manually pull one or two custom cables through the pipes. Each of these cables carries 216 hair-thin glass strands sheathed in Kevlar and polyethylene to seal out hungry rodents and corrosive sewer gases. The robots then staple the cables to the pipe roof.

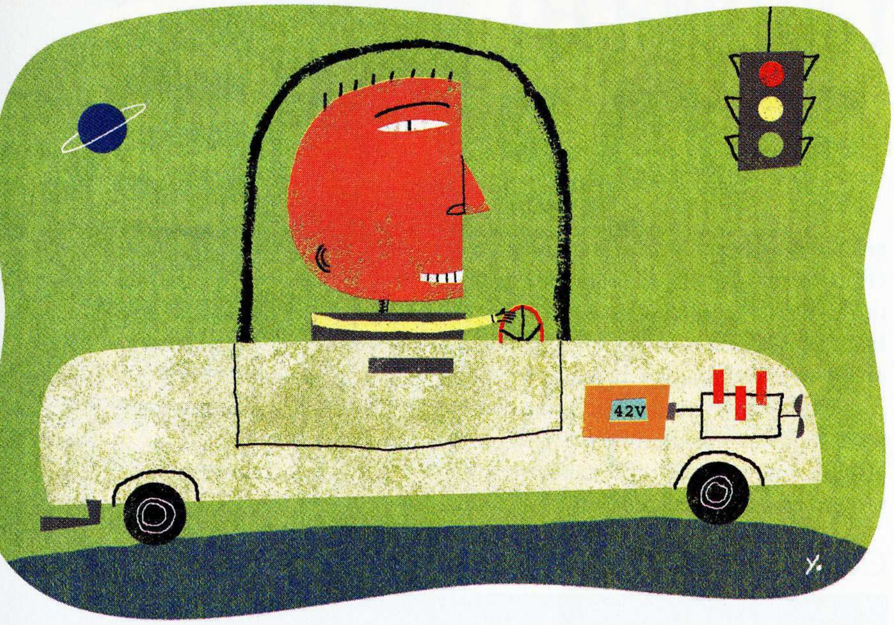
Toronto-based Stream Intelligent Networks is testing Robotics Cabling's system in Toronto and is laying plans to deploy it across Canada, while CityNet is in full swing using KA-TE's robotic systems to install fiber-optic cables in several U.S. cities, including Omaha, NE, Albuquerque, NM, and Indianapolis. Both firms are targeting bandwidth-hungry office buildings, whose 20- to 25-centimeter-wide sewer pipes accommodate today's pint-sized robots.

Robot designers, on the other hand, are tackling the even smaller pipes and the tight turns that lead to individual homes. A residential campaign may be imminent: KA-TE says its researchers have already used robots to install fiber to three homes in Japan.

—Peter Fairley



COURTESY OF CITYNET TELECOMMUNICATIONS



JAMES YANG

The Electronic Car

TRANSPORTATION | Advanced automotive electronics used to mean digital dashboard displays or electronic fuel injection. But carmakers are now moving toward a full electronic embrace of basic systems ranging from valve timing to steering. To provide the needed juice, they are adopting a new 42-volt electrical system, replacing the 14-volt standard that has reigned since 1955.

Ford Motor was first to make a public commitment with its January announcement that the Explorer sport utility vehicle will include a 42-volt system in 2004, initially enabling a new combined starter/alternator. The engine would shut off at every red light; a tap on the gas would fire the starter/alternator, moving the Explorer forward while rapidly restarting the engine. Ford predicts dramatic fuel economy gains.

Ford isn't alone in trying to revamp the internal combustion engine with electromechanical components. Also hard at work are General Motors, DaimlerChrysler, BMW, Toyota and Renault. "Virtually all of the important manufacturers and suppliers have signed on to 42-volt," says David Perreault, an electrical engineer at MIT's Laboratory for Electromagnetic and Electronic Systems. The lab leads an industry consortium developing the technology, which will require new electrical systems and batteries.

Mercedes-Benz (now part of DaimlerChrysler) helped launch MIT's 42-volt initiative in 1995 and is one of several companies developing one of its toughest applications: electromechanical engine valves. Such systems would replace today's mechanical systems and provide super-efficient combustion control, including shutdown of individual cylinders while others continue operating, saving fuel. A Mercedes spokesman offered no predictions, but Perreault expects electronic valves to reach drivers within a decade.

Other possibilities include electronic steering, which would eliminate the power-robbing steering pump and allow a computer to intervene if a driver's jerky maneuver threatened a rollover. More immediately, luxury cars need extra juice to power new electronic trimmings like onboard navigators. **—David Talbot**

Tumor Tracker

CANCER | **Brain tumors called glioblastomas are among the most vicious of cancers. So when Harvard University pediatrician Evan Snyder's best friend, Jim Galambos, developed a glioblastoma in 1996, Snyder set out to attack the disease, using an unusual tool: neural stem cells, special cells capable of developing into new neurons and other brain structures.**

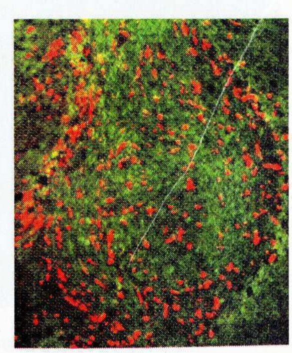
Based at Children's Hospital, Boston, Snyder had already used these cells to treat such inherited diseases as Tay-Sachs in mice. Stem cells tend to migrate throughout the brain, settling in damaged areas and initiating repair. Maybe, Snyder mused, they could find the areas damaged by glioblastomas, which also spread widely, and deliver drugs to the cancer cells. Galambos's illness was a strong motivator. "I promised the kids and...his wife that I would dedicate my efforts to helping him," says Snyder.

Galambos didn't make it, but Snyder's work has since borne fruit. In recently reported mouse experiments, Snyder showed that genetically altered neural stem cells could hunt down brain tumors, delivering a protein that activates an anti-cancer drug—and dramatically shrinking the tumors. The experiments "succeeded beyond my wildest dreams," says Snyder. Glioblastomas have historically been impossible to eradicate because they diffuse wildly in the brain.

But the therapy still faces serious obstacles. In humans, the stem cells themselves could theoretically generate harmful masses; conversely, they might fail to reproduce and thus allow the tumor to evade treatment. The immune system might attack the stem cells as invaders. Snyder says there's no evidence of any of these problems in mice, but mice are notoriously poor predictors of results in humans.

If all continues to go well, a clinical trial of the glioblastoma treatment could begin within two years, with the help of Sunnyvale, CA-based Layton BioScience, which has licensed Snyder's stem-cell technology.

—Ken Garber



Stem cells (red) invade a tumor.

COURTESY OF EVAN Y. SNYDER

Gene Babel

BIOTECH | Small DNA-laden wafers have transformed biology. Using these DNA chips, geneticists can see which genes are turned on, or expressed, in a cell at a particular time. Such gene expression experiments allow bioscientists to diagnose different diseases, quickly screen thousands of drug candidates for efficacy and safety and even learn the functions of newly discovered genes.

Sharing this information over the Web could lead to an explosion in biological knowledge. But each experiment generates gigabytes of data written in one of several formats, depending on the type of chip used. And with dozens of chips on the market and hundreds of ways to analyze the data, the Web is in danger of becoming a genetic Tower of Babel.

Companies and academics have begun creating uniform formats for representing gene expression data, designed to work on any computer *(see table)*. Overseeing the effort to fashion a single standard from these proliferating formats is the Object Management Group, an international nonprofit consortium that has helped the computer industry establish software standards for over a decade. A life sciences subgroup formed in 1997, and standards for protein and DNA sequence analysis followed. Next in line: molecular and chemical structure representations and drug trial data, as well as gene expression data.

Participants hope that a gene expression standard will emerge by year's end. If it does, the enormous amount of data produced in the wake of the Human Genome Project could find a common language on the Web. **—Erika Jonietz**

Gene Standards Projects

GROUP	PROJECT	PURPOSE
Rosetta Inpharmatics	Gene Expression Markup Language	Data representation
European Bioinformatics Institute/Microarray Gene Expression Database Group	Microarray Markup Language	Data representation
National Center for Genome Research	GeneX/GeneXML	Database/data representation
NetGenics	Standard interface for gene-expression data warehousing	Data management and analysis

Nanodot Lasers

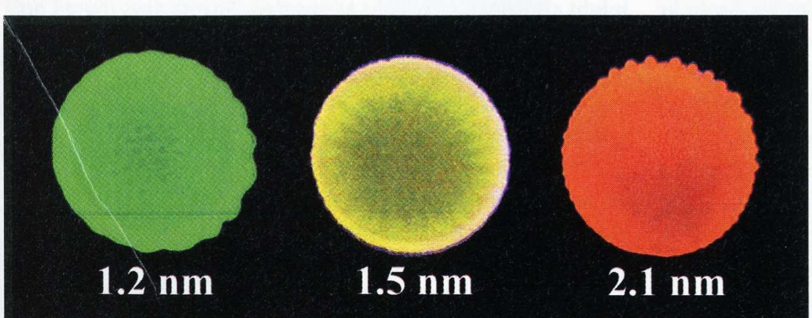
OPTICAL NETWORKS | Make particles of semiconductors small enough—just a few nanometers across—and they glow in a dazzling range of colors. These nano particles are known as quantum dots, because quantum effects tune the color of the glow to the size of the particle—a phenomenon that scientists have seized upon to make exquisitely sensitive biomedical assays *(see "Quantum Dot Com,"* TR *January/February 2000)*. In theory, these tiny glowing particles could also be a boon for optical networking by providing lasers and amplifiers that work in a wide range of frequencies. But for over a decade experts have been trying to fashion quantum-dot lasers, with little success.

Now MIT chemist Moungi Bawendi and Victor Klimov, a laser expert at Los Alamos National Lab in New Mexico, may have stumbled upon the solution. Klimov and Bawendi discovered that when the dots are stimulated with a powerful pump of light, most of them fritter away the energy as heat in less than one-millionth of a second. But if the dots are crammed close enough together, photons released by neighboring dots arrive in time to trigger additional photons from a nanodot before the energy dissipates. A dense film of cadmium selenide dots that Bawendi prepared for Los Alamos did the trick, generating a cascade of photons.

Bawendi has since fashioned this cascade of light into a laser and has started to tweak the dots to make the beam more efficient. Success could free optical networks and other laser-dependent technologies from today's limited spectrum of beams. For starters, quantum-dot amplifiers could extend long-range transmission of fiber-optic signals to wavelengths of light outside the narrow band of infrared beams served by today's amplifiers. "The colors are essentially limitless," says Bawendi.

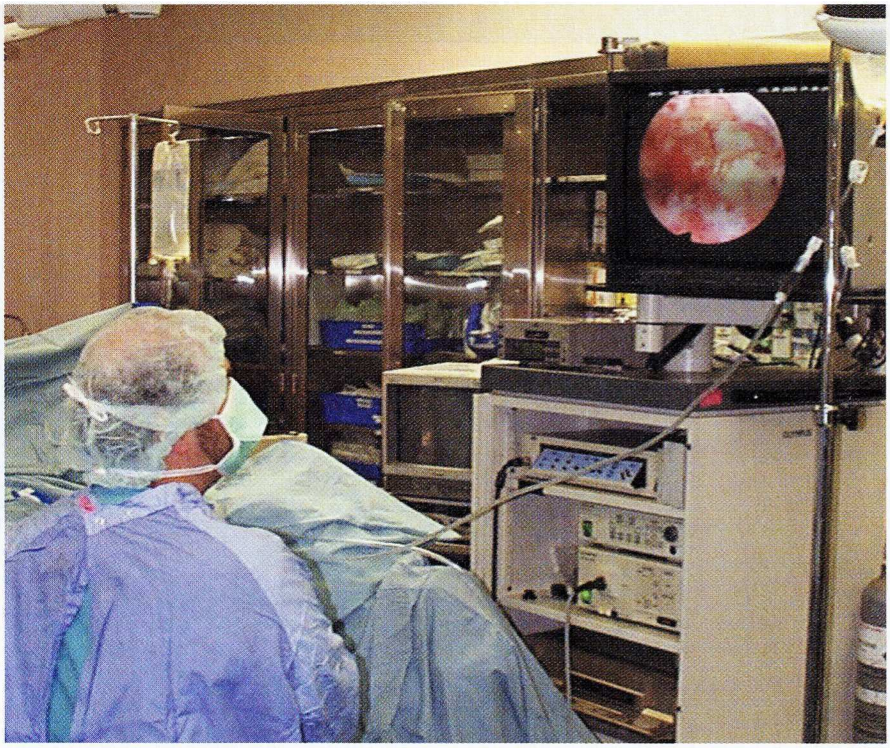
If the scientists are right, the future of quantum dots in expanding the possibilities of optical communication could be bright, indeed.

—Peter Fairley



COURTESY OF VICTOR KLIMOV

Three films, each made of different-sized cadmium selenide quantum dots. A film made of dots 1.2 nanometers in diameter glows green, while a film of 2.1-nanometer dots glows orange.



COURTESY OF STEVEN F. PALTER

Watching the Body

Endoscopic HDTV gives surgeons better vision

SURGERY | Consumers have been slow to buy into high-definition television (HDTV) despite the technology's promise of sharper, brighter images. Now the makers of a prototype HDTV system are looking for a better reception from an audience a bit more demanding than your average couch potato: surgeons. The hope is that using the technology in endoscopic surgery could lead to quicker, more accurate surgeries with fewer complications.

Endoscopes allow surgeons to see into the body to perform complex surgical procedures, from repairing joints to removing cancerous lesions, through tiny incisions. Each endoscope has a thin tubular protrusion that can be threaded through the incision; the tube houses lenses or optical fibers that feed images from inside the body to an eyepiece, or to a camera that relays the picture to a monitor. Although surgeons perform hundreds of thousands of such procedures every year in the United States alone, they often lament the poor quality of video due to blurring and transmission artifacts.

Steven F. Palter, a surgeon at the Yale University Schooi of Medicine, spurred electronics giant JVC to join with San Ramon, CA, medical optics company TTI Medical to make a mini-HDTV camera for endoscopic surgery. Recently, JVC developed a palm-sized HDTV camera—the world's smallest—for microsurgery on tiny blood vessels and nerves. The next challenge was adapting the camera to an endoscopic viewing system.

With 1125 scanning lines, compared to the 525 lines offered by current video standards, the surgical images derived from the HDTV system had more than twice the resolution, and the digital processing of the signal eliminated almost all visual artifacts. "It's like looking with your naked eye into the body," says Palter, who has successfully used the system in five procedures so far.

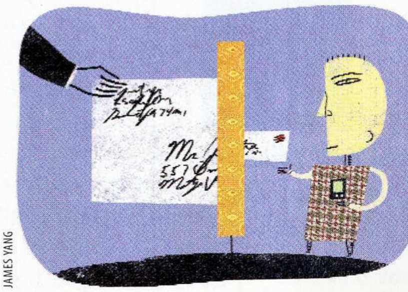
The potential benefit is not simply a clearer picture but a vastly improved perception of detail. Surgeons will be able to more readily distinguish between normal and abnormal tissue, and to conduct operations requiring fine dissection more accurately. "There are areas that could not be seen with a traditional video system that you can clearly see with HDTV," says Jay M. Cooper, a Phoenix gynecologist and president of the American Association of Gynecologic Laparoscopists. "I see potential for dramatic improvements in what we can offer our patients." JVC and TTI Medical are working to make the camera smaller still, with improved sensitivity and easier sterilization. They expect it to be commercially available by the end of the year. **—Marc Wortman**

Inbox on a Diet

INTERNET | A couple years ago, Brandeis University computer scientist Jordan Pollack received an e-mail with a seven-megabyte file attached. Frustrated by how long it took to download the file, Pollack created a system to automatically strip attachments from e-mail and put the files on a Web site, replacing them with a Web link. This "thinned down" his e-mail inbox, so Pollack called his creation Thinmail. He liked the idea so much that, in 1999, he launched a company to bring it to market.

Pollack says the Waltham, MA-based company's system is "just more polite than sending huge attachments." But it could change the way people use Palm Pilots, cell phones and other mobile devices to check e-mail. With little memory to spare, these systems normally discard attachments. But Pollack created an "e-mail bot" to allow users to manage the files, which the Thinmail system stores on its own server. An attachment can be sent to a nearby fax machine for printing, forwarded to someone else, or, for certain file types such as Microsoft Word and HTML, translated to plain text and its first 100 lines returned to the mobile user for viewing. The system currently handles over 30 standard Windows, Mac and UNIX file types; future plans include support for scanned documents and voice messaging.

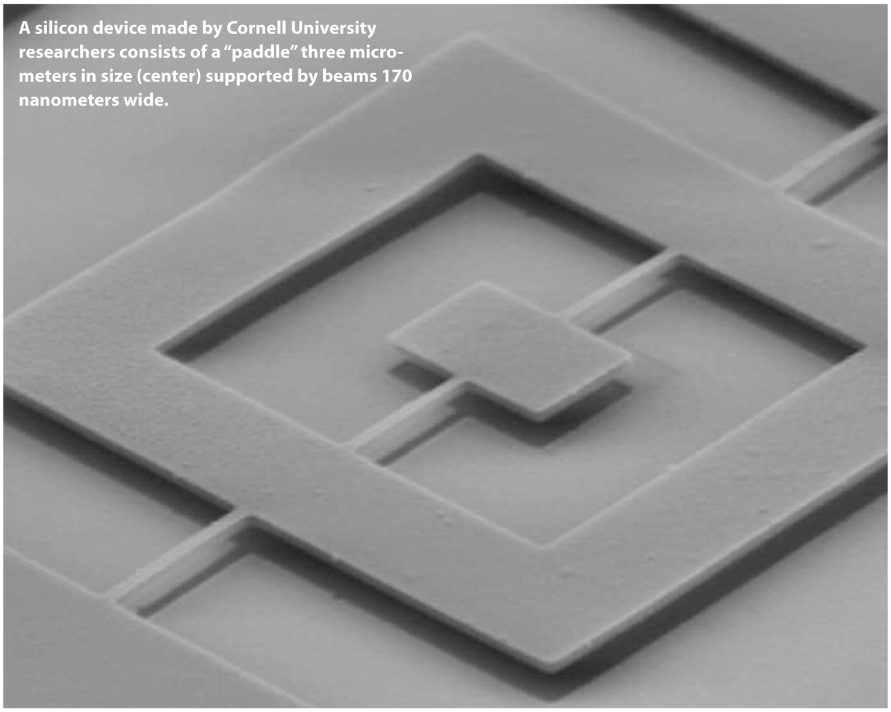
Thinmail charges users via a micropayment system based on storage space used—storing a 10-megabyte file for one day, for example, costs five cents. The company signed up its first customer last September; as of January, it had over 350 users. —Erika Jonietz



JAMES YANG

UPSTREAM

SPOTLIGHT ON A HOT TECHNOLOGY TO WATCH



A silicon device made by Cornell University researchers consists of a "paddle" three micrometers in size (center) supported by beams 170 nanometers wide.

COURTESY OF CORNELL UNIVERSITY

NEMS: Machines Get Tiny

Nanoelectromechanical systems begin to flex their muscles

ULTRASMALL MACHINES ARE everywhere these days. Tiny mechanical devices, so minute that a hundred thousand could sit on a pencil eraser, are responsible for triggering your airbags during an accident, spitting colors out in precise detail on your inkjet printer and projecting light in the newest digital theaters. Made with the same silicon fabrication methods used to crank out computer chips, microelectromechanical systems (or MEMS) have over the last decade become well embedded in the high-tech landscape.

Now engineers and physicists are taking the next step in machine miniaturization, building mechanical devices on the nanometer scale (a billionth of a meter). If the researchers succeed, their work could lead to ultrasensitive sensors that can detect even the most subtle genetic alterations responsible for a disease, or to ultrastrong artificial muscles that might replace damaged human tissue or power tiny robots.

This next frontier in mechanization is called nanoelectromechanical systems (or NEMS). "With MEMS, you could make a mirror and it was still a mirror, just smaller," says physicist Harold Craighead, who directs the Nanobiotechnology Center at Cornell University. "But with NEMS, the whole interaction of matter with light is different. You get completely new physical properties, and that's a big opportunity for new devices."

Why is small so beautiful? For one thing, you can pack more devices into a given space. It's the same idea behind making smaller and more powerful computers by squeezing tens of millions of transistors onto a semiconductor chip. But nanomachines offer special advantages. For one thing, they operate at the same size scale as biological molecules (a DNA molecule is about two nanometers in diameter), allowing the devices to directly interact with biological systems.

A simple vibrating cantilever underpins many nanomachines. With electron beams and chemical etches, researchers carve away the material around a finger of silicon, leaving one end anchored in the substrate. As any mechanical engineer can tell you, this bar will have a well-defined resonant frequency—it will be, in essence, a Lilliputian tuning fork. Nearly anything that affects the vibration frequency of the cantilever can be detected. Add a little extra mass, and the lever will decrease its resonant frequency, making it a highly sensitive mass balance. "With nanometer cantilevers we estimate we can detect a mass change of a single atom," says Jim Gimzewski, a leader of the IBM Zürich Research Lab's program in nanomechanical devices.

Others are building nanomachines out of tiny hollow pipes called carbon nanotubes *(see "Wires of Wonder,"* TR *March 2001).* At Honeywell Labs in Morristown, NJ, materials scientist Ray Baughman and his coworkers have fabricated a sheet of aligned nanotubes that bends in response to an electrical charge. In the jargon of mechanical engineering, the sheet can act as an ultrastrong actuator, a mechanical device for moving or controlling something. Nanotubes outperform natural muscle and in theory could top even the most powerful ceramic actuator materials. The scientists also discovered that the nano device can, like other actuators, act in reverse; in that mode, the mechanical bending is transformed into electrical power. Baughman envisions that sheets of aligned nanotubes could be placed in the ocean like fronds of seaweed, with the wave motion used to generate electrical power.

The day when such nanomachines become as prevalent as the microscale versions remains years off. But those who have observed the unfolding of the micromachine revolution say the nano research is well worth keeping an eye on. "Nano today is where MEMS was 10 years ago," says Al Pisano, a professor of mechanical engineering at the University of California, Berkeley, who headed the U.S. Defense Advanced Research Projects Agency's MEMS program from 1997 to 1999. "I've watched MEMS go from what some people thought was a farce to dead serious startup companies with major investment. Nano is a tougher game to win, but we've got a lot more resources and momentum now." —**David Voss**

WORLDCOM

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generation d

In Africa, Patents Kill

FOR THE BIGGEST, GRAVEST, most consequential intellectual property fight of our times, look no further than access to lifesaving drugs in Africa. The scourge of AIDS on that continent is already shaking traditional notions of patent rights to their foundations. Posterity may judge our age by how we respond.

The facts in this global face-off could not be more harsh.

On one side are the desperate and dying. According to the United Nations, over 2.4 million Africans died from AIDS last year in a pandemic that, if unchecked, will claim more lives than the Black Death that swept Europe in the 14th century. But this is not even the worst part of the story. While some 25 million Africans carry HIV today, fewer than 25,000—one-tenth of one percent—currently receive drug treatments that could save or at least prolong their lives.

On the other side in this life-and-death battle, in the gold-plated jerseys, are the giant, multinational pharmaceutical firms—GlaxoSmithKline, Merck, Novartis, Pfizer, to name a few. They are some of the world's most profitable companies. According to one estimate, sales for the top 10 U.S. drugmakers exceeded manufacturing costs by $100 billion last year. These technological titleholders have the awesome power and resources to save many of Africa's AIDS victims. All they have to do is ease their choke hold on their intellectual property. But even a modern-day plague of unthinkable proportions has yet to loosen that grip.

To their credit, last year the world's biggest drug firms did announce plans to cut prices in some African countries and even give some drugs away to the Third World nations hardest hit by AIDS. More telling, though, is what they haven't done: condone the sale of generic copies of their lifesaving products to the world's neediest patients. In Ghana, GlaxoSmithKline has even moved to block the sale of generic copies of one of its AIDS drugs. It is a reprehensible and misguided strategy that will produce no good.

If there's a lightning rod in this debate, it is Yusuf Hamied, chief executive officer of Cipla, India's largest drug manufacturer. Last September, Hamied announced that his firm, as a public service, could distribute generic versions of the most-needed AIDS medications at a tiny fraction of the cost charged by the patent-holding companies.

In AIDS-stricken Africa, the enforcement of Western drug patents is a needless death sentence for millions.

Cipla's offer was not idle. While India has strong patent protection in many sectors, it has maintained lax patent regimes in agriculture and drug manufacturing to aid its poor and encourage indigenous industry in these vital sectors. As a result, drugs cannot be patented in India. This allows companies like Cipla to reverse-engineer bestselling products with impunity and legally sell the knockoffs cheaply at home.

Not surprisingly, the pharmaceutical giants have long viewed Cipla as a pirate and a global threat. Because these firms thrive off their R&D fruits, they guard their intellectual property ferociously. They dread nothing more than a cascade of generic copies and falling prices.

It's easy to see why. Take, for example, Pfizer's miraculous, patented antifungal agent Diflucan (fluconazole). Some 10 percent of Africa's AIDS sufferers need a daily tablet of this drug to stave off the lethal brain inflammation cryptococcal meningitis. Pfizer, which sells this drug in the West for $25 or more per pill, has laudably agreed to give some away in South Africa. But it has only halved its price elsewhere on the continent—still far beyond the financial reach of most who need it. Cipla sells it in India—legally—for 64 cents.

Under normal conditions, the drug manufacturers could rightfully object to powerful free riders like Cipla. But given the crisis at hand, these firms need to view things differently. They should applaud Cipla for stepping into the breach where they will not. There is little threat to business; with its feeble price reductions, Big Pharma is certainly not selling many high-priced drugs in Africa anyway. And many, many people are dying.

The roles of pirate and hero can be reconciled. What's needed is a way to carve out an exemption to patent protection during bona fide epidemics. There are plenty of analogies to draw on. The world over we let ambulances ignore red traffic lights as they rush to respond to emergencies. Even more pertinent, in times of catastrophe we allow public officials to declare "states of emergency" that replace some normal rules of the road with a more germane set. In the face of a regional crisis like the one in Africa, perhaps the World Health Organization could make a similar designation—encouraging the temporary suspension of IP rights in the region so that, on an emergency basis, any willing drugmaker can distribute its lifesaving wares at cost.

AIDS in Africa has surely reached epidemic proportions. It's time to stop business as usual and declare an IP state of emergency. ◊

Deutsche Banc Alex. Brown

MERGERS AND ACQUISITIONS

Bluestone SOFTWARE **$525 million** Has been acquired by Hewlett-Packard January 2001	manugistics **$358 million** Has acquired Talus Solutions December 2000	element 14 **$594 million** Has been acquired by Broadcom November 2000	LYCOS Europe **€961 million** Has acquired Spray Network October 2000	SMALLWORLD **$212 million** Has been acquired by GE Powersystems October 2000
NTT Communications **$5.5 billion** Has acquired Verio September 2000	CDNOW **$134 million** Has been acquired by Bertelsmann August 2000	VASTERA **Undisclosed** Strategic alliance and merger with Ford Motor's U.S. customs operations August 2000	DIGITAL INSIGHT **$140 million** Has acquired AnyTime Access July 2000	NATURAL MicroSystems **$155 million** Has acquired InnoMediaLogic July 2000
ASK PROXIMA **$518 million** Has been acquired by InFocus Corporation June 2000	Peregrine SYSTEMS **$2.0 billion** Has acquired Harbinger Corporation June 2000	Buhrmann **Undisclosed** Sale of Information Systems Division to Specialist Holdings Group May 2000	connecta **$1.6 billion** Merger with Information Highway AB May 2000	C-PORT. **$430 million** Has been acquired by Motorola May 2000
MANDATOR **$1.4 billion** Merger with Cell Network AB April 2000	cnet **$736 million** Has acquired mySimon, Inc. March 2000	Maker Communications, Inc. **$1.4 billion** Has been acquired by Conexant Systems March 2000	yesmail.com **$721 million** Has been acquired by CMGI March 2000	flycast **$2.5 billion** Has been acquired by CMGI January 2000

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Companies are poring through the medical heritage of large populations searching for the genes behind common diseases. The effort could revolutionize medicine—and is already triggering controversy.

your genetic destiny for sale

BY GARY TAUBES

Large extended families have traditionally been the mother lode of genetic research. From them came a precious commodity: links between the presence of a disease and the errant genes responsible for it. When medical researcher Nancy Wexler, for instance, went looking for the genetic cause of Huntington's disease in 1979, it was a 9,000-member Venezuelan family that enabled her to trace the telltale patterns of disease inheritance.

Wayne Gulliver's family is not nearly so large, but it is impressive nonetheless. Until two years ago, when his great-great-aunt passed away, six generations of Gullivers were alive in Newfoundland. His grandmother, who died last October, had some hundred descendants, while his parents, only in their 60s, already have 26 grandchildren to go with their 10 children. All of this would be professionally irrelevant if Gulliver's family were not typical of Newfoundland, and if Gulliver himself, a dermatologist who studies the genetics of psoriasis, were not involved in a rapidly emerging discipline called population genomics, the goal of which is to identify the underlying genes responsible for common chronic diseases, such as cancer and heart disease.

ILLUSTRATIONS BY BRIAN CRONIN

If these efforts **succeed**, they could revolutionize the nature of drug discovery

Two years ago Gulliver met Paul Kelly, CEO of the British company Gemini Genomics, which had already assembled a huge international network of twins to use in searching for gene-disease associations. Gulliver pitched Kelly the idea of supplementing Gemini's database with population statistics from Newfoundland and Labrador. His selling points were simple: a population of 550,000, of which almost 90 percent are descended from the original Irish, Scottish and English immigrants who arrived before the mid-19th century. It is, Gulliver says, a population in which the locals often know their family lineages back to the original immigrants. "Not like the States," he says, "where you have three kids, send them off to college, and you might be lucky if you see each other every fifth Thanksgiving."

And many of those families, like Gulliver's own, are large. In such a tightly knit population consisting of large extended families, common diseases might run in recognizable patterns—shared by siblings, for instance, or passing through paternal or maternal lines, or linked to other distinctive physical characteristics. All it would take to mine this rich vein of medical history for valuable clues to disease-causing genes would be a sufficient effort, some very advanced biotechnology tools and some startup capital.

Gulliver's pitch prompted Gemini to launch Newfound Genomics in February 2000. In the near term, Newfound Genomics aims to concentrate on diseases endemic to the local population—psoriasis, diabetes, obesity, inflammatory bowel disease, osteoporosis and rheumatoid arthritis—with the hope, considering the Irish/English/Scottish ancestry, that any relevant genes or gene variants that might be uncovered would play significant roles in other populations. The expectations behind the company are anything but modest, at least judging by the inaugural press release. "We have the potential here to develop a major international powerhouse of clinical genetics," said Kelly, "that will provide benefit not only for the Newfoundland and Labrador community but also patients suffering from these diseases worldwide."

Newfound Genomics is just one of a host of such ventures formed over the last few years *(see "A Database Sampler," p. 46)*. The specifics vary from project to project, but the strategies are similar: sift through the DNA of large populations, if not entire nations, in hope of identifying the underlying genetic causes of those diseases most likely to kill us. The researchers, pharmaceutical company executives and venture capitalists involved are all betting that recent advances in biotech and computing have made it possible to take a few hundred or thousand victims of a disease, analyze their DNA, compare it to the DNA of healthy individuals and identify the salient differences—those genetic variations that result in illness on the one hand and health on the other.

If these efforts succeed, they could revolutionize the nature of drug discovery and medical treatment. In the ultimate manifestation of this technological dream, no hypothesis of disease causation is necessary. Medical researchers need not speculate first about what biochemical pathways are involved or what proteins are at fault, which is the laborious way that medicine now makes progress. Instead, they would simply compare databases of genetic samples and disease records, employing computerized data-mining operations to find the causative genes and gene variations at work. Pinpoint the genes that predispose individuals to disease and you have a clue to what disease mechanisms are at work and how to prevent or repair them.

The same kind of research would also provide clues to what your own medical future has in store for you—what afflictions are more or less likely to do you in; what treatments, pharmaceuticals or preventive measures will most likely ward off disease or cure it; and perhaps even how you personally should lead your life to maximize the chance of surviving to a ripe old age. Are you genetically predestined, for instance, to fall dead of heart attack in your 50s or fade slowly away with heart failure in your 90s? Will breast cancer or Alzheimer's be your fate? Schizophrenia or depression? Diabetes?

This endeavor is what Stanford University geneticist Neil Risch, for one, calls "the endgame of human genetics." Certainly it is the best shot of geneticists to identify the genes at play in the common ills of mankind. Should it work, it "will herald a new era of information-based targeted care, in which genetic profiling will identify the disease predisposition risks faced by individuals and, if disease occurs, will make it possible to tailor therapy based on individual patient needs," wrote George Poste, former chief scientist for SmithKline Beecham (now GlaxoSmithKline), in the journal *Nature.* And even if it doesn't achieve such lofty goals, it may still provide new understanding of the nature of common chronic disease.

In the jargon of genetics, the search for disease-causing genes is a search for the genotype that explains the phenotype. Genotype is the individual variations in the three billion base pairs of DNA and the tens of thousands of genes we all share; it's our actual genetic makeup. Phenotype is how that DNA physically manifests itself—in this case, as the susceptibility to disease, or the progression of disease, or the susceptibility of the disease itself to treatment, all of which likely have a genetic component. Genotype goes into a black box of human biology and phenotype comes out. Occasionally this connection is excruciatingly deterministic, as it is, for instance, with Huntington's disease or cystic fibrosis, in which a single mutation in a single gene means you have the disease or will get the disease. In the vast majority of human ailments, however, the connection is excruciatingly vague—as it is with personality or intelligence or athletic excellence or any other complex trait. When geneticists use the word "complex," they mean that more than one gene is responsible for an individual's condition, and probably quite a few.

The challenge for the geneticist is, depending on how you look at it, a signal-to-noise problem or a needle-in-a-haystack problem. With tens of thousands of genes in the haystack of the human genome, how do you identify those one or two or 10 that play a role in any particular disease?

This is where large families come in handy. Because all the members share a common genetic inheritance, it's highly likely that any disease that runs in the family is caused by the very same genes and the very same mutations slipped into the family gene pool by a distant ancestor. If you can find a few hundred family

members with the disease and a few hundred without, you can be pretty confident that eventually you'll find the mutation that is present in the DNA of the afflicted members and absent from the DNA of the healthy ones. For researchers, this is much simpler than the situation where the afflicted are unrelated, since in that case the genetic causes may also be unrelated, and the overall variation in the DNA so bewildering that the signal from any disease-causing genes is overwhelmed by the background noise of genetic variation.

In the early 1980s, researchers turned to large extended families and a technology known as linkage analysis to begin systematically searching for disease-carrying genes. By following the pattern of disease inheritance in large families and linking the presence of the disease to known genetic markers—long regions, for instance, in which the DNA letters A and C alternate repeatedly—geneticists could first localize the disease-causing gene to a specific chromosome or specific chromosomal region. They would then employ a technique called positional cloning to scour the nearby DNA for the genes and finally identify a particular misspelling that led to disease. The techniques were developed in "a spectacular series of discoveries," says MIT geneticist David Altshuler.

But success didn't come easy. Nancy Wexler, for instance, started her search for Huntington's in 1979. By 1983, using blood samples sent from Venezuela, her colleague James Gusella of the Harvard Medical School had narrowed the position of the Huntington's gene to a short tip of chromosome four that was *only* a million base pairs in length. It took another 10 years to identify the gene at work and nail down the critical mutation.

Since then, geneticists have identified hundreds of disease-causing genes, using ever faster methods of testing DNA samples, ever faster computers and a new generation of software to compare and contrast DNA variations. The sole caveat in this remarkable accomplishment is that virtually every gene identified, with a few exceptions, has been for a disease caused by a single gene and a single mutation. These are rare diseases—like Huntington's or cystic fibrosis—because evolution strongly selects against them. When geneticists used the same techniques to look for the genetic causes of common chronic diseases like heart disease and cancer, success was considerably harder to come by.

That these common diseases have a degree of "heritability" is undeniable. But the last decade of mostly negative studies is compelling evidence that the underlying genetics is indeed complex. It may be the interaction of two or three genes and gene variants that predisposes an individual to a specific chronic disease. It may be considerably more—each having a minor effect on the likelihood of contracting the disease or the eventual outcome.

This complexity makes the search for chronic-disease genes extremely difficult. If the impact of any one gene is so small—say five percent as opposed to the 100 percent of the Huntington's gene—then following the connection through the black box becomes that much more difficult amidst the noise of environmental factors and other genes. "You might be looking for a combination of three or 10 or 100 genes," explains Altshuler, "each of which might have multiple mutations in it that might affect the disease, and all of them collaborating with the environment and perhaps randomness or fate. So the correlations will be much, much weaker. It means you need different tools to augment the search. In particular, it means you have to look at lots of people. Imagine if one gene causes the disease; you might look at as few as five or 10 families, each with lots of people, and be able to pick out the correlation. The numbers don't have to be that large to make a compelling case. If no single gene or mutation is going to explain more than five or 10 percent of the disease, you need hundreds or thousands of people."

Indeed, solving the puzzle would probably be impossible if not for the recent advances in the computer and lab technologies used to determine the genotypes of individuals. In addition, the Human Genome Project now provides a map of the entire three billion base pairs that constitute the human genome. "A necessary step,"

says Altshuler, "is to know what the genes are and have very fast and efficient tools for finding variations and asking, does this variation correlate with a disease? Now the Human Genome Project provides a list of all the genes, and that is fundamentally empowering. Even in the previous paradigm, where the disease, like Huntington's, was caused by a single gene of big impact, you had to find all the genes in the local region, characterize them and figure out which one has the variation. That would take an army of people. The Human Genome Project has come along and done a lot of that labor up front."

For the pharmaceutical industries, geneticists, and venture capitalists, the immediate challenge is to find a population that will provide sufficient numbers of disease victims, the clinical data necessary to accurately identify the disease, and the opportunity to take DNA samples from everybody involved. Picking the right population is a choice of trade-offs. The bigger the population, the greater the sample size and the better the statistics, but the more difficult and expensive it becomes to get accurate clinical data. Large extended families will likely share very similar disease-causing genotypes, which makes it easier to identify the relevant genes, but those mutations or gene variants might be specific to the family and rare in other populations.

The effort to achieve the right balance among these trade-offs has led groups to various strategies for setting up and exploiting the information contained in large medical databases. In contrast to Newfound Genomics, some have shied away from looking at closely related populations. Cambridge, MA-based Genomics Collaborative is, for instance, recruiting physicians and letting them enter patients on a disease-by-disease basis. This network is growing at the rate of 7,000 new patients every month, says CEO Michael Pellini. Eventually, he says, the company hopes to have genotype and phenotype data on a half-million patients, representing "large heterogeneous populations."

This kind of population, Pellini argues, will offer up gene-disease associations—and the diagnostics and pharmaceuticals that might come out of them—with an applicability to large, diverse populations. Pellini cites BRCA1, one of two genes associated with familial breast cancer. When the gene was first identified, he says, "People thought it would be implicated in a very significant number of women with breast cancer. When follow-up studies were conducted to validate that association, it was realized that BRCA1 is actually implicated in less than 10 percent of women with breast cancer. One of the reasons that occurred is the researchers started with small studies and with homogenous populations. Think about it. If you develop a diagnostic that is based on one population, one thing you know is that it's representative of that one population. You have no idea if it's representative of any other populations. Our goal is to come out with the diagnostics that are actually representative of a very broad population, and ultimately, to develop therapeutics with the exact same rationale."

At GlaxoSmithKline, the working philosophy of Allen Roses, who heads the genetics program, is to pick the diseases, recruit the world experts on those diseases, and then let the experts recruit the patients, first from families with a history of the disease, and then from what are known in the lingo as "sporadic" cases—those isolated cases without a family history. GlaxoSmithKline is building eight "clinical genetic networks," each for a different chronic disease, and Roses estimates that each network will cost $8 million for the first three years. "It ain't cheap," he says. "It is not high throughput to work up the data patient by patient, family by family, control by control. It is the part of the study which no technology can circumvent. It is the slowest part. But what you get out of it, if you put in the effort, is the polymorphisms [specific gene variations] of specific genes that *are*—not 'could be,' not 'might be,' not 'we believe'—but *are* clinically associated with the disease."

DESPITE THE OPTIMISM, THE POPULATION GENOMICS BOOM has the potential to become mired in two distinct controversies—one ethical, the other scientific. The ethical debate was ignited three years ago, when former Harvard University neurology professor Kari Stefansson collected $12 million in venture capital and returned to his native Iceland to launch deCODE genetics, with the dream of mining Icelandic DNA for disease-causing genes *(see "Population, Inc.," p. 50)*.

To Stefansson, the Icelandic population represents an incomparable genetic resource. Virtually all the 280,000 inhabitants are descended from the Vikings who landed in the late ninth century. And this inbred population comes with excellent medical records beginning in 1915. As a result, Iceland represents a population in which finding underlying disease-causing genes should be as easy as it gets. Indeed, the potential in terms of new drugs is so great that in February 1998 deCODE signed a deal with the Swiss pharmaceutical giant Roche that could potentially be worth $200 million over five years.

Controversy, however, erupted in the spring of 1998 when the millennium-old Icelandic parliament took up consideration of a bill that would grant deCODE the right to construct a national health-records database of the entire Icelandic population. The bill gave deCODE a 12-year exclusive license to run the database and sell access to third parties, which would include any other scientists who might want to use the records.

The bill was sprung on the Icelandic community "as lightning from the clear sky," says Einar Arnason, a population geneticist and evolutionary biologist at the University of Iceland. Arnason is also vice chairman of Mannvernd, the Association of Icelanders for Ethics in Science and Medicine, which was formed to oppose the bill. While the act was passed by the Icelandic parliament in December 1998, Mannvernd is challenging its constitutionality and counting among its allies the Icelandic Medical Association and a substantial fraction of the nation's physicians.

DeCODE's critics have attacked it on several ethical fronts, charging it with misleading the Icelandic public; playing on Icelandic patriotism and national self-interest, when the company is incorporated in Delaware and backed almost exclusively by U.S. investors; and, as Harvard University geneticist Richard Lewontin wrote in the *New York Times*, converting "the health and genetic status of the entire population into a tool for the profit of a single enterprise."

The specific criticisms are threefold: first, that deCODE will have exclusive rights to the data in the health-records database,

while other scientists, even Icelandic ones, will have to buy their way in; second, that the company may not be able to adequately protect the privacy of individuals whose records go into the database; and third, and most controversial, that the deCODE database works on the basis of "presumed consent" rather than "informed consent." In other words, rather than asking individuals beforehand whether they would like to participate, deCODE has a right to the records of anyone who doesn't "opt out" by filling out a form and sending it in to the proper authorities.

The deCODE imbroglio has almost single-handedly rendered the ethics issue a primary focus in the emerging field of population genomics. As medical ethicists like Stanford law professor Henry Greely point out, genetics research grew up with family studies, in which the families involved have an obvious incentive to participate. "They want to find something to help themselves, their kids, their grandkids," he says. "They're not worried about who makes money, and they end up with really close relationships with the geneticists." Now that the research is moving into entire populations, says Greely, "Researchers don't have any contact with anything but ones and zeroes or perhaps a little bit of extracted DNA." Issues such as whether or not participants should be told about findings that relate directly to their own health, and even whether they should benefit financially, have to be worked out carefully in advance.

If nothing else, the ongoing deCODE controversy has the other players in population genomics trumpeting their ethics policies—and how they differ from deCODE's. UmanGenomics, for instance, was founded in 1999 to market the genetic information from a 15-year-old bank of biological samples taken from the bulk of the population of the county of Väterbotten in northern Sweden. Sune Rosell, a former Karolinska Institute pharmacologist and now

A Database Sampler

COMPANY	POPULATION
Newfound Genomics (Newfoundland, Canada)	550,000 Newfoundlanders
Autogen (Melbourne, Australia)	180,000 Tonganese
deCODE genetics (Reykjavik, Iceland)	280,000 Icelanders
UmanGenomics (Umea, Sweden)	260,000 Swedes
DNA Sciences (Fremont, CA)	100,000 Internet users
Wellcome Trust/Medical Research Council	500,000 U.K. volunteers

president of UmanGenomics, explains that three levels of informed consent are involved in the endeavor, from the individual level (an informed consent form is signed before anyone donates blood samples) to a societal level (all projects have to be approved by a regional ethics council) and a community level (representatives from the county are on the company board). In addition, says Rosell, while the company is privately owned, 51 percent of the shares are held by the county and the local University of Umea.

In Britain, the Wellcome Trust and the governmental Medical Research Council are planning to create the U.K. Population Biomedical Collection to link DNA samples, medical records and lifestyle details from 500,000 volunteers. The project has been approved for funding, but the only significant work so far, says project leader Tom Meade, who also directs the Medical Research Council's epidemiology and medical-care unit, has been "a great deal of public consultation" on "all the issues of reassuring people about confidentiality and getting informed consent. And making sure people understand what this is all about."

In the United States, public opposition has already scuttled at least one venture. Boston University, which runs the famous Framingham Heart Study, recently founded Framingham Genomic Medicine, a privately owned company *(see "Medical Records, Inc.,"* TR *July/August 2000)*; the plan was to generate a database linking 52 years' worth of meticulously detailed medical records from the Framingham Heart Study to genotype data, which the Framingham researchers began collecting in the late 1980s. The company then hoped to market access to the database as a resource to pharmaceutical companies and other academics. In December 2000, however, the university decided to kill the company when it couldn't make headway on the ethical issues—in particular, the fact that the study was funded over the decades by the federal government, and academics had always had access to the information free-of-charge.

Next to the tangled ethical issues, the scientific controversy is straightforward: a debate between optimists and pessimists, with the bulk of the community falling somewhere in between. The pessimists argue that the genetic nature of chronic diseases—whether asthma, heart disease or diabetes—is unlikely to be simple enough for association studies to elucidate. And if the number of genes is large, and the effect of each gene is small, or if multiple genes confer similar traits—say, resistance to heart disease or cancer—then the studies are likely to turn up little or nothing real, or, at least, nothing real and useful.

The optimists, on the other hand, are betting that two or three or a handful of genes play a large enough role in many chronic diseases that the research will find them. Even optimists, however, recognize that for population studies to find disease-causing genes, the number of genes responsible for susceptibility to any particular common disease must be relatively low. (Though where there's only one, the family studies to date should have unearthed it.) How many more than one is the question. "There is a lot of room between one and infinity," says Stanford's Risch.

And the farther from one the answer lies, the less successful these association studies will be. As Risch points out, the only way to find out which side is right is to do the scientific research on which genomics companies are betting. "I don't know what else we can do in terms of human genetics to try to find genes for common diseases," says Risch. "Most people believe there's a genetic component to these diseases. If it turns out to be too many genes, and the effects are too modest, that will kill it. But there's no way to know right now, and I don't see any reason not to be optimistic. This has not played out at all, not by any stretch of the imagination." ◊

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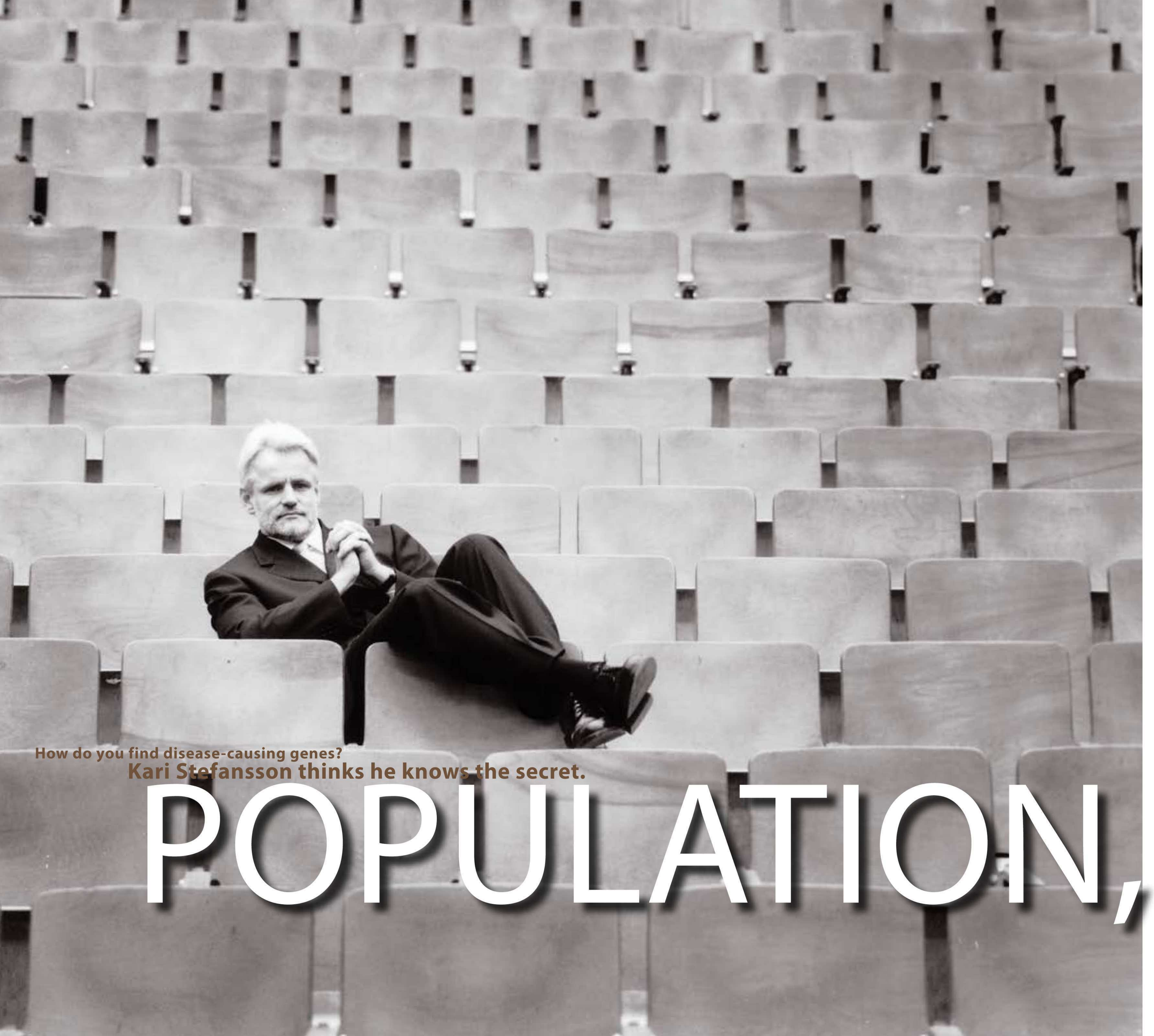

How do you find disease-causing genes?
Kari Stefansson thinks he knows the secret.

POPULATION, INC.

Q & A

KARI STEFANSSON IS IN A HURRY. THE PRESIDENT AND CEO OF deCODE genetics must get across town to see a former colleague at Beth Israel Deaconess hospital before dashing to the airport—and he still needs to squeeze in a promised interview with a journalist. In the cab, he alternates between discussing travel plans in Icelandic with a coworker and expounding on the intersection of disease and human evolution in English with *TR* associate editor Erika Jonietz.

Changing how genetics is done has kept Stefansson on this hectic pace since 1996, when he left Harvard Medical School and Beth Israel to found deCODE genetics, based in his native Iceland. In 1997 the company proposed construction of the first "phenotype database," a collection of the health records of all 280,000 Icelanders. DeCODE would use information from this centralized health-care database and Iceland's extensive public genealogy records to find disease-causing genes, aided by the relatively homogenous genetics of Iceland's population. This plan helped launch a revolution in population genomics *(see* *"Your Genetic Destiny for Sale," p. 40)*, with a variety of other companies quickly following suit.

Although it's widely imitated, deCODE remains controversial. Editorials in publications from the *New York Times* to the *New England Journal of Medicine* attacked and defended the ethics and scientific merits of the proposal. After extensive public debate, Iceland's parliament approved the creation of

PHOTOGRAPHS BY JOHN SOARES

the Icelandic Health Sector Database in December 1998 and granted deCODE a 12-year license to create and operate the database last January. A vocal minority, including the physician-led group Mannvernd, is still trying to stop the database in the courts, but deCODE has moved ahead. Last July, the company completed a successful initial public offering that raised $244 million.

TR: You were a professor at a leading medical school. Why leave and switch directions so radically to found deCODE?
STEFANSSON: Basically, the methods of genetics are the methods that you use no matter the disease you are studying. Around the time I founded deCODE, the technology had evolved to the extent that it had stopped being the limiting resource; the limiting resource was becoming the access to populations to do this work. So I moved to a place where there were the least limitations on that resource. I think the Icelandic population is not unique, but it's very well suited to do exactly what we want to do, which is to apply this new technology to a well-defined population.

TR: What has it been like for you to be a CEO instead of an academic scientist?
STEFANSSON: The difference between the two is vastly overrated. What mostly drives you is the desire to win, to perform, to control your own fate, whether you do it through money, or the admiration of people who follow your work or whatever. It's a larger scale: I was running a lab of 10 or 15 people; I'm now running a company of about 450 people. But it is basically the same thing. You put together certain ideas, you gather around you people to execute them. The fact that you can create value out of the results of your research doesn't alter in any way the weight or the importance of the fundamental question you are asking.

Also, don't forget that I come from Iceland. My family has lived in Iceland for 1100 years. There is a certain adaptation that has taken place. We fit this sort of wet, barren, dark corner of the North Atlantic. That does not necessarily mean I like every aspect of it, and I miss America a lot. It was a great place for me; this was a community that was extremely generous to me. I learnt an awful lot here. I'm running a company in Iceland that is fundamentally run on American philosophy. It fits pretty well there.

TR: What specifically motivated you to create a phenotype database?
STEFANSSON: When you look at common diseases, they are probably common because they are complex, and they're complex for all kinds of reasons. Not only because they probably require the confluence of many genes to cause the disease, but they may also require interactions between genes and the environment. And when you are studying complex common diseases, you have to work on the assumption that you know very little. In spite of 75 to 100 years of intense research into these diseases and an enormous expenditure of money, we have come a short distance in developing a useful understanding of these diseases, simply because the fundamental approach just doesn't reach deep enough. You don't see enough of a pattern to put together a reasonable hypothesis. You basically have to begin to use systematic data mining, to be able to bring together large amounts of information.

TR: How does a phenotype database help you find the genes behind diseases such as asthma, heart disease or diabetes?
STEFANSSON: You may have someone with diabetes in your grandfather's generation and it skips the parents and then it affects the children, and so on. And to study these disorders, you have to go to a population, because once a disease begins to skip generations, a nuclear family isn't a useful unit of society to study.

We can design experiments to mine knowledge out of this [population] data by putting together hypotheses, the old intuitive approach. But as beautiful as that approach is, it is not very powerful. The alternative is to use combinatorial analysis, to take every single data point and compare it to every other data point, looking for the best fit, unblinded by a hypothesis. The unaided human mind cannot handle large numbers of data points; you need the modern computer. It's an extremely powerful approach. And I'm absolutely convinced that we will revolutionize the ability to develop knowledge about the common diseases by using systematic data mining.

TR: What is deCODE's advantage in this field?
STEFANSSON: We have the genealogy of the entire nation [of Iceland] on a computer database. When you're studying the genetics of disease, you're not only studying the information that goes into making an individual; you're also studying the flow of this information from one generation to the next. And the genealogy gives you the avenues by which the information flows.

TR: Have you had any success yet?
STEFANSSON: We have indeed had success. We have been able to map genes in incredibly complex diseases, like osteoarthritis, osteoporosis, schizophrenia and psoriasis. Every single complex disease that we have applied significant effort to, we have been able to map by using this process. When we were starting our company, we put most of our effort into development of software systems, of algorithms to analyze data, and we were ahead of the biology that we subsequently began to look at. Making use of informatics, mathematics, and all these genealogical approaches, we have been able to solve problems that others have had difficulties with. Then we are taking the discovered genes and turning them into drug targets. And we are already working on the development of drugs on the basis of those targets.

TR: What kinds of drugs is deCODE working on?
STEFANSSON: We have set up a division to work on drug development, which will probably be located in the States for human resources reasons. It started out as a cell biology division where we work on the biology of the genes we discover. Since we are working on the genetics of 60 diseases now, we have the possibility of selecting the things that are easiest to work on. I honestly cannot tell you which genes we plan to target, because we haven't made any final decisions. Remember, if you are speaking in terms of drug development based on basic biological discoveries, it takes about 12 to 15 years from the time you make a discovery until you have a drug on the shelves.

TR: How does all this fit into deCODE's business model?
STEFANSSON: We are basically market-

"IN SPITE OF 75 TO 100 YEARS OF INTENSE RESEARCH INTO THESE DISEASES AND AN ENORMOUS EXPENDITURE OF MONEY, WE HAVE COME A SHORT DISTANCE IN DEVELOPING A USEFUL UNDERSTANDING OF THEM, SIMPLY BECAUSE THE FUNDAMENTAL APPROACH JUST DOESN'T REACH DEEP ENOUGH."

ing three lines of business: a discovery service, from discovery of genes to the discovery of drug targets to the discovery of drugs; the service component, which is the database that is based on putting health-care information in the context of genetics; and software systems, not only to use in discovery but also in the delivery of health care. When we started our work and we looked around, there were no software systems that would allow us to do genetics at the scale that we wanted to do it, so we put together a very large informatics section. They have put together algorithms and programs that do spectacular things when it comes to large-scale genetics, for genotyping [finding the individual variations in genetic makeup], for mining genes from raw sequences, for doing statistical analysis.

We have also put together a software system to prevent medication errors, problems due to drug interactions and things of that sort—a very smart, very elegant program. We have put together software systems that protect privacy not only in discovery work but also in the delivery of health care. Now, and particularly in the future, people will be sending medical information to institutions left and right in electronic form. To do that, you need to put a shell around the data so you can protect privacy. We have also been putting together a clinical decision-support system. All of this grew out of our focus on the database.

TR: Who are the customers for your various products?
STEFANSSON: The discovery stuff goes mainly to pharmaceutical companies and diagnostics companies. The database services, to academic and other kinds of health-care institutions. The software systems we are marketing to health-care providers, the pharmaceutical industry, biotech companies, software companies. The breadth of customer is considerable. This is not just biotech companies serving pharmaceutical companies.

TR: There has been a lot of controversy surrounding deCODE's creation and licensing of a database containing the health records of every Icelander.
STEFANSSON: The database has been controversial mostly for the wrong reasons. There are all kinds of reasons to be skeptical of collection of personal information, and I think that we can never be too careful when we do that. But most of the controversy was focused on misinformation, the insistence that we were working on biological samples without informed consent and things of that sort.

TR: How do you reassure the public of the value of these databases?
STEFANSSON: There is no question in my mind, nor in the mind of anyone who has looked at this carefully, that this is an extraordinarily important approach, and people should take it. The only question is, What is the price? What are the sort of ethical and societal dilemmas that you have to overcome to be able to take this approach? If you're going to do a large study that involves a large number of people, a whole population, you have to establish some sort of a consensus in the population whether it should be done—what some people call community consent. In Iceland, people took my suggestion to do this sufficiently seriously that the parliament passed a law. We could easily have done it without a law, but the parliament passed a law. There was a societal debate that lasted for nine months. There were 700 articles written in the country's three newspapers; there were 140 television and radio programs addressing this. It was probably the most debated issue in the history of our republic, and on the eve of the parliamentary vote, a poll showed that 75 percent of people supported the bill, 25 percent were against. And now, under one and a half years after the bill was passed, there was another poll taken showing that the support had risen to 91 percent.

But societal or community consent is not enough. You have to have some sort of consent at the level of the individual: What is the "how" of the collection of this data? Does it comply with current practice in the use of health-care information? By law in Iceland, the information in this database is only information produced in the process of delivering health care, nothing else. Permission to cross-reference it with information from DNA is entirely dependent on an explicit informed consent from those who have given us DNA.

TR: How does this differ from the way information is usually collected for medical research?
STEFANSSON: Health-care information is going to be collected with presumed consent [in which permission is assumed and must be specifically refused], and there's not a single place in the world where people use information produced in the process of delivering health care with anything except presumed consent. There is not a single significant study in your country where people have demanded informed consent for the use of information produced in the process of delivering health care. So this is exactly in keeping with that, and before you decide anything else, you should think about the consequences of demanding informed consent for secondary use of health-care information. It's a serious decision, because you would not be able to do epidemiology as we do it today. If it had been required in the past, we wouldn't have the health-care system that we have today; there's no question about it. When you come today to seek health care, you're using the consequence of the fact that your parents and their parents allowed the use of their health-care information. Simply to discover knowledge. And if you refuse to do the same, you're going to

"THE WAY TO DEAL WITH ANY RISK FROM KNOWLEDGE IS NOT TO FORBID ITS DISCOVERY, OR THE GATHERING OR STORAGE OF INFORMATION; IT IS TO REGULATE HOW YOU USE IT."

diminish the probability that your children and their children will have health care of the same quality.

TR: How do you collect the genetic information you need to cross-reference with the health-care data so that you can actually map genes?

STEFANSSON: We have to get informed consent from people to give their blood, to isolate the DNA, to genotype and then cross-reference that with health-care information. We have so far been collecting DNA simply on the basis of individual diseases we have been studying, and we have DNA from about 50,000 Icelanders. We may go ahead and collect DNA systematically, put an ad in the newspaper and ask people to give blood for this purpose. And actually that would be the least invasive method to obtain DNA. When you're doing it through physicians who take care of patients and relatives of patients, there is a certain coercion involved because you're approaching people at a moment of at least perceived need. But eventually, because everyone has a disease and everyone has someone in their family with disease, we would have everything we need to do this systematically, even if we would simply approach them on the basis of diseases.

TR: It would seem risky to have the medical information of every person in the country collected in a central database. For example, people in the United States tend to worry about insurance companies using such information to deny them health-care coverage. How do you take advantage of the potential that lies in this systematic data mining without causing too much danger?

STEFANSSON: I have visited about 25 countries this year, and in every country I come to, I take out my ATM card and withdraw money. I can do that because the entire world is a network of centralized databases of personal information on finance. And the only restriction on my access to your bank account lies in this little card I have. It is much easier to abuse personal information in finance than in health care. You actually have to have a fairly lively imagination to figure out how you can abuse it [in health care]. But the reason we have electronic banking is that we feel it provides such comfort to us that we're willing to compromise on protection. I'm absolutely convinced that less than one percent of the people in this world would believe that the use of electronic banking is a more noble goal than discovering new knowledge in medicine.

TR: How would you address people's concerns about this, though?

STEFANSSON: The way to deal with any risk from knowledge is not to forbid the discovery of the knowledge, or the gathering or the storage of information; it is to legislate or regulate how you use it. There are so many reasons to have centralized databases in health care. The one in Iceland can only be used for discovery, and that is unfortunate, because if you have centralized databases in health care, you can provide so much better health care. A colleague of mine, his car hit a tree a couple of years ago and he was seriously wounded, he almost died. When he was brought into the hospital, after he had been peeled out of his car, the hospital knew nothing about him except his name. Imagine if they would simply have been able to put his name into a centralized database and get all the health information there was on him, his parents, his siblings. The power of this is enormous, and are you going to say that we should deny ourselves the opportunities that this brings with it because there may be kooks out there who would want to abuse this? The only kooks that could abuse this would be the kooks in the insurance industry. We can simply regulate that. ◊

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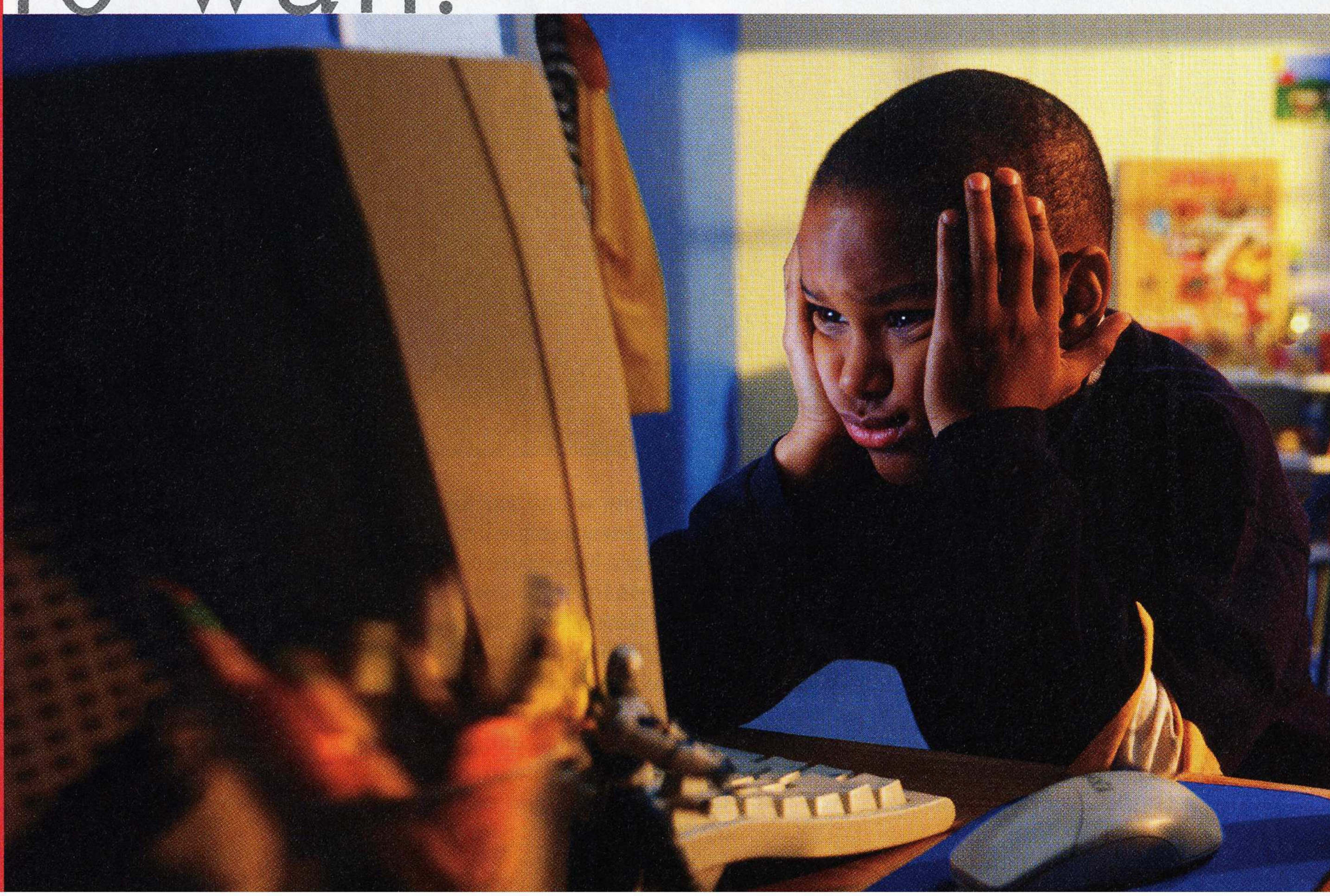


The Universal Cell Phone

BY DEBORAH SHAPLEY

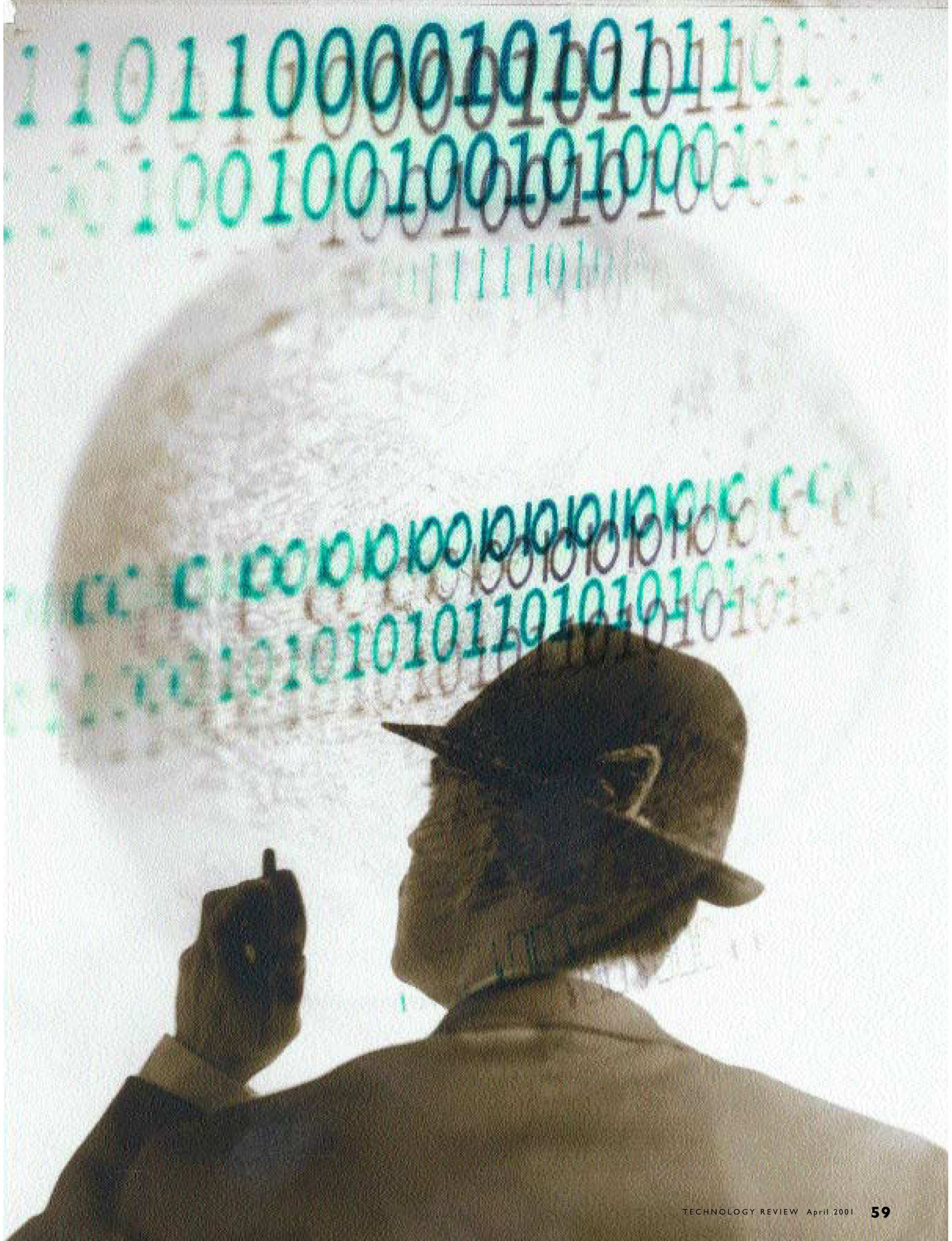
Mobile phones work only in some areas, and they become obsolete rapidly, as new features are developed. Flexible software in phones and wireless networks could change all that.

THE GREAT WIRELESS REVOLUTION, WHICH TOOK OFF WITH THE SPECTACULAR spread of cell phones in the 1990s, and which is supposed to bring broadband Internet to the gadget in your pocket, is in trouble.

Demand is soaring, forcing makers of wireless equipment and network operators to invest billions to meet humanity's inexhaustible thirst for getting connected anywhere, anytime. Global sales of mobile phones soared from seven million in 1990 to 700 million last year and are projected to reach 1.7 billion in 2005. More and more users expect their phones to deliver very clear voice signals and to pick up their e-mail, albeit slowly.

But as frustrated callers know, communicating with mobile phones is tricky. The problem: today's wireless networks use a maze of incompatible transmission standards, so road warriors aren't guaranteed a dial tone when they travel. U.S. wireless operators alone use three competing standards, and just one of these is compatible with the leading standard in Europe, which itself has several variants. Most Asian wireless networks are built to another standard. This radio-wave Babel prevents most mobile phones in the United States from being viable elsewhere. It also limits U.S. manufacturers' economies of scale against foreign competitors.

ILLUSTRATIONS BY STEPHEN SHEFFIELD



The wireless revolution's troubles go beyond conflicting standards. Consumers consistently expect more advanced features, so models that were state of the art in, say, 1995 will seem antique by 2003. By then, almost all new mobile phones will offer some form of Internet access. Millions of people in Japan, for example, snapped up i-mode, a service that lets them use cell phones to send text messages, buy stocks and check sports scores. Worldwide, companies are spending billions to build a new network, usually referred to as "third generation," or 3G, that is expected to bring broadband—detailed Web pages, music, even video—to your mobile phone.

However exciting for consumers, these advances carry a price, since there's currently no easy way to upgrade mobile phones, or the base stations that carry their signals to the network, without changing hardware. Moreover, the wireless industry can't predict which offerings will be winners; the consequences of failing to guess right can be devastating. Last year, European wireless operators spent heavily to offer phones equipped with a format known as Wireless Access Protocol, only to find the buying public impatient with their slow download speed. Demand was limp.

Small wonder that wireless companies are looking for ways to make their networks flexible, so as to avoid costly retrofitting as demand changes. A technology first developed by the military and now being pursued by several technology leaders could be the key. The technique is known to experts as software-defined radio, or SDR. ("Radio" refers here not to AM or FM, but to any equipment that communicates through the airwaves on radio frequencies, as cell phones do.) The advantage offered by this new approach is that it shifts the workload of wireless units from dedicated components to software that can be reprogrammed to work on a different standard or add applications. That's entirely different from today's mobile phones and base stations, in which virtually all signal processing is carried out by electronic circuitry designed to do one and only one thing.

The migration toward wireless networks that are adaptable due to their use of reprogrammable software "is one of the most important trends in technology today," says analyst Craig Mathias of MobileInsights in Mountain View, CA. James Gunn, of the Dallas-based consulting firm Forward Concepts, calls this trend the "revolutionary next step" that wireless technology needs.

Flexible software could also help solve another basic problem for the whole wireless enterprise: scarcity of spectrum (or bandwidth). As the demand for wireless communication explodes, there is an accompanying dearth of the necessary frequency channels. The Federal Communications Commission recently concluded that networks using reprogrammable software could ease that shortage because they could seek out and use temporarily unoccupied channels. Last December, the FCC proposed rules for its licensing of equipment and software in order to speed up U.S. adoption of the technology.

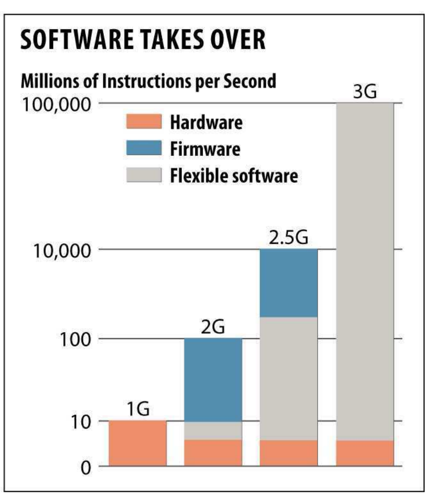
More like a PC

The first cell phones relied on dozens of hardware components. In the past 15 years, programmable chips have been added, but their function is set immutably at manufacture. Today, dedicated, single-purpose chips do most of the work in mobile phone handsets and base stations; these chips are made as simple as possible to keep costs down.

Given the mishmash of conflicting standards and the uneven advent of the next generation of broadband wireless, manufacturers such as Motorola are starting to see dedicated components as a liability. A manufacturer that guesses wrong about the future standard will find itself with a lot of useless junk in its warehouses. As Ken Riordan, of Motorola's Personal Communications Sector in Libertyville, IL, puts it, "If you commit your solution to hardware, and you get it wrong, then you're going to be in a very jeopardized situation."

Today's cell phones rely on single-purpose chips. Guess wrong about a future standard and a company will have a lot of useless junk in its warehouses.

So more-general-purpose software that can be reprogrammed looks appealing. No one understands the trade-offs better than Joseph Mitola III, a radio engineer whom many insiders perceive to be the central innovator in the field. Early in life, Mitola became fascinated with computer code; he learned Fortran while attending high school in Providence, RI, in the 1960s. When he got to college—Northeastern University in Boston—he says he was "one of the few who knew how to program anything." Mitola had also tinkered with radios. Combining both interests led to a career creating top-secret radio designs for the military—including the first software-defined radios, which were for military use *(see "The Military Seed," p. 61)*. Indeed, the commercial wireless industry learned of the technology in the early 1990s mainly through Mitola's papers and lectures. His military bosses cleared these for public release, figuring the military could benefit if the commercial world pushed the technology further and brought costs down.



BETSY HAYES

Successive generations of wireless technology (denoted by "G" numbers) will shift more processing into software.

The problem Mitola was trying to solve was similar to the situation that would arise if you had to put a new circuit board in your PC every time you wanted to do a different task—say, switch from Web browsing to a spreadsheet. You'd eventually run out of space inside the box. The same holds true for cell phones. "If you want to cram in four more functions, it means each device has to be about a quarter the size it was before," says Mitola, now at the McLean, VA, office of MITRE, a nonprofit R&D consultancy. But, he adds, chips aren't shrinking rapidly enough to make that possible, given the many standards and functions the wireless revolution demands.

If mobile phones and their base stations *were* computers, new software could

download easily through their wires. But wireless communication is fundamentally different. Mobile phones must push signals across the airwaves at precisely the right power level and in the exact transmission format. They must be tuned to receive incoming, powerful signals from one or more channels. Antennas catch irregular analog signals traveling through space on "carrier" frequencies; incoming radio signals must then be converted to an intermediate frequency through combination with another radio wave produced inside the receiver. Then the carrier wave gets subtracted to put the signal in baseband—that is, a power level and speed that ordinary digital processors can handle. While the signal is in baseband, it is translated into a stream of binary ones and zeroes, which are in turn decoded, decrypted and formatted into voice or data.

The first operations to benefit from reprogrammable software are operations in the baseband. In one model of Motorola base station, for example, the software that performs the baseband coding and decoding is reprogrammable, according to Motorola's Riordan.

Next, manufacturers would like reprogrammable software to handle the intermediate-frequency and radio-frequency parts of the job. That's a more difficult technological challenge, in part because silicon—which is by far the most common and least expensive chip material—does not handle radio-wave signals well. Radio-frequency processing of broadband signals will most likely use gallium arsenide chips running 100 *billion* instructions per second, compared to the roughly 10 to 100 *million* instructions per second in single-purpose chips in present-day phones.

The rise in computing complexity is exacerbated by the push to send signals much faster. So-called third-generation broadband wireless service could move data at two megabits per second, a roughly hundredfold leap from the operating speeds of most of today's wireless networks. All these demands mean chips will require lots more power; added power is far more easily obtained in a base station than in a small, lightweight mobile phone.

Still, Mitola says he would like to see a mobile phone that "digitizes the whole signal at the antenna" across widely spaced frequencies. "Then," he adds cheerfully, "other software can do whatever it wants with it." Such a flexible phone, he says, will be able to sniff out unused channels in the spectrum. Several U.S. chip makers, including big players Texas Instruments and Analog Devices, are pushing to develop the enabling technology. Small firms such as QuickSilver Technology of Santa Clara, CA, and Morphics Technology of Campbell, CA, are also vying for the prize.

To start with, however, manufacturers are putting reprogrammable chips mainly into base stations that relay signals from cell phones to the network. Unlike handsets, base stations have few space or power constraints. For instance, Lucent Technologies, second to Motorola as a supplier of wireless base stations worldwide, has new models that are "smart" (that is, they have a flexibility endowed by software) at the antenna. According to Paul Polakos, director of the company's advanced wireless technology lab in Whippany, NJ, the new base stations can shift among multiple channels, assuming different "personalities" depending on which type of communication is called for—analog or digital voice transmission, high-speed data, or broadband.

Cramming this kind of software-derived flexibility into

The Military Seed

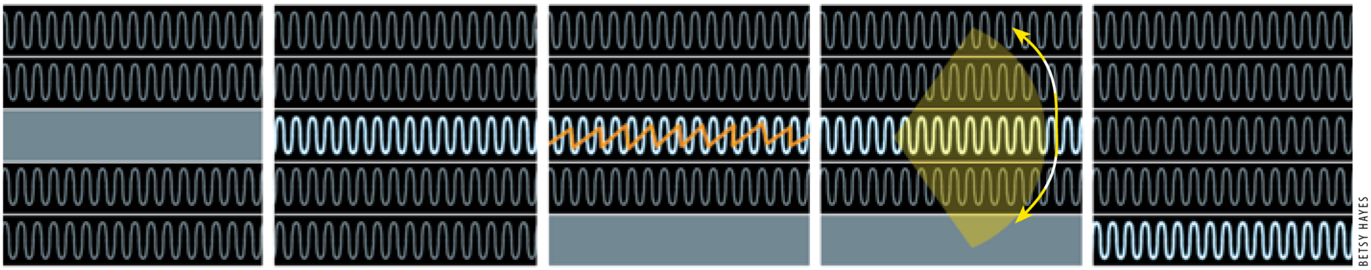
The notion of controlling most operations of wireless reception and transmission with software evolved during the Cold War. The military needed receivers that could scan the spectrum, sense incoming signals from enemy aircraft or ships and react with countermeasures on the same frequencies. Though this military equipment was heavy and armored—not to mention expensive—one developer, E-Systems in Dallas, saw the commercial potential. When the Cold War ended, the company and its clients at the Pentagon allowed public release of basic principles.

That wasn't the end of the military's role in developing this technology. In post-Cold War operations, different armed services needed to be able to work together more closely, due to budget limitations and because wars were most likely to take place in more confined theaters. The U.S. Defense Advanced Research Projects Agency began the SPEAKeasy project to see how reprogrammable software could help the myriad military radio systems talk to each other. The Naval Research Laboratory, meanwhile, has produced a chameleonlike "information terminal" now used on board some Army vehicles. This system can adopt any of 12 radio "personalities" from software stored in memory.

Although DARPA works with big defense contractors, much of its largesse is directed at universities. Among its projects on flexible software communications technologies is MIT's SpectrumWare project. Vanu G. Bose's research on this project led him to found Vanu, which markets flexible radio designs to the military and law-enforcement agencies.

One DARPA project foreshadows the "cognitive radio" networks prophesied by MITRE radio engineer Joe Mitola. The Small Unit Operations: Situation Awareness System is intended for ground troops entering hostile or empty terrain with no available communications. According to DARPA program manager Paul Kolodzy, troops will be able to "communicate clandestinely in buildings, jungles and mountainous terrain." Their wireless transmitters and receivers will sniff out available spectrum and then form an intelligent network that might be totally independent of the local authorities' radio systems, and possibly independent of other U.S. military radio systems operating in a theater. The wireless devices would know where they were, even when "reliable Global Positioning Satellite fixes are not available." How do they do that? Don't ask.

Wireless Rent-A-Channel



At any given moment, any of several frequencies might be available for temporary use. Here, the middle band is for "rent." **The cognitive cell phone starts using this frequency at a rental rate it negotiates with the owner of the channel.** **A warning signal from the channel owner (e.g., fire department) warns the cell phone to move off.** **The cognitive cell phone immediately starts searching for a new frequency to rent.** **Having found a newly available band (bottom), the cell phone begins transmitting at that frequency.**

lightweight handsets will not be easy. Even Mitola admits that "truly breakthrough technology" will be needed for a lightweight handset to flex among three or four frequency bands and operational modes. Meanwhile, smart, software-programmable wireless sets will find their way into vehicles, which can accommodate larger and heavier systems than people's pockets can. Indeed, one early use of flexible software radio technology will be in radios in police and fire vehicles: public safety agencies' wireless systems are notoriously incompatible. The FCC is encouraging public agencies to adopt this technology. Several firms, such as Vanu of Cambridge, MA, are developing equipment for this market.

Future Phones—Smarter Still

Wireless devices that morph through different "personalities" on the fly would be a boon to their users. But at the same time they create policy problems, as new technologies that cross boundaries often do. Historically, the FCC authorizes each piece of equipment for a type of use and specific channel. How should the regulators license mobile phones and base stations that can readily be changed after they're in use? How free should third parties be to load new software into your phone? How will it be possible to distinguish legitimate upgrades of the network from rogues trying subvert it?

The FCC decided that rules to cover these scenarios were not needed—yet. But it also concluded it should facilitate this technology's evolution. A main reason is the lack of enough spectrum for third-generation wireless services in the United States at present. So equipment that sniffs out and utilizes unused swaths of spectrum could alleviate what the FCC calls the U.S. spectrum "drought."

To do this, however, will require both base stations and handsets to become supersmart—a leap to what Joe Mitola calls "cognitive radio." A cognitive device will not only scan its spectral environment; it will also have built-in memory and maps and positioning capabilities. Those will enable it to react intelligently to its environment.

Over the past two years, Mitola built a crude civilian version of a cognitive radio as a doctoral project for Sweden's Royal Institute of Technology. When this device is outdoors, it configures itself to use the prevailing cellular phone protocol; when carried indoors it switches to the format of the building's local area network. Mitola explains that a more advanced version could "know" that the person carrying it is in trouble and send a distress signal on the local emergency frequency to give rescuers its location.

But mobile phones that reorient to a new channel for temporary use would have to get permission to "rent" that spectrum for some period of time from the official licensee. In a paper that foreshadowed his doctoral thesis, Mitola proposed a payment system that would employ the signal protocols *(see illustration above)*. Using such a system, your intelligent handheld would scan the spectrum to find a channel that was not in use at the moment; for example, it might find one that the local fire department had the license to use but was offering for rent. Your radio would bid to rent the channel. The fire department's radios, receiving the bid, could agree—or wait for other bids. But the instant the station's bells rang and the firemen needed their channel back, their radios would bump the renter off. Mitola reckons the channel's owner could regain control in 25 milliseconds—a delay that would be unnoticeable to human speakers. Your cognitive mobile phone would sign off, reckoning and paying a bill for time used, then start scanning for another open channel.

The FCC, in endorsing this vision, has joined forces with an unlikely ally: George Gilder, self-styled seer of the "telecosm" and critic of the FCC for holding back innovation. For years, Gilder has predicted that intelligence will grow at the edges of the wireless telecom network with the result that channels become fluid. Wireless devices and networks that employ flexible software, he says, will "transform the entire world of wireless communications," the way personal computers transformed wired networks.

The swaths of spectrum that are most commercially desirable are often referred to as prime beachfront property. But Gilder wants people to stop thinking of spectrum as some kind of ethereal analogue to physical land. "Smart radios suggest not a beach but the endless waves of the ocean itself. You can no more lease electromagnetic waves than you can lease ocean waves."

Making that ocean available to billions of people could be one impact of flexible software-based wireless networks. But even before we reach this nirvana of spectrum abundance, the technology could make wireless networks more cost effective and future-proof—and keep the wireless revolution rolling. ◊

TR100 NOMINATION FORM

Technology Review is seeking nominations for its 2002 edition of the "TR100"—one hundred young men and women who are making significant contributions to emerging technologies that will have a profound impact on our world. Nominees must be under age 35 on January 1, 2002, and their work should exemplify the spirit of innovation. *Technology Review* will profile each finalist in a special January 2002 issue, and recognize them at a gala dinner and awards celebration. Thank you for your nomination!

NOMINEE*
INSTITUTION
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PHONE*
E-MAIL*
AGE*

TECHNICAL AREA OF NOMINEE'S WORK:

BRIEFLY DESCRIBE THE NOMINEE'S WORK SO FAR:

WHY DO YOU THINK THIS PERSON MIGHT BE ONE OF THE TOP 100 YOUNG INNOVATORS?

PLEASE PROVIDE CONTACT INFO FOR OTHER REFERENCES (UP TO 3) FOR YOUR NOMINEE:

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RELATIONSHIP TO NOMINEE:

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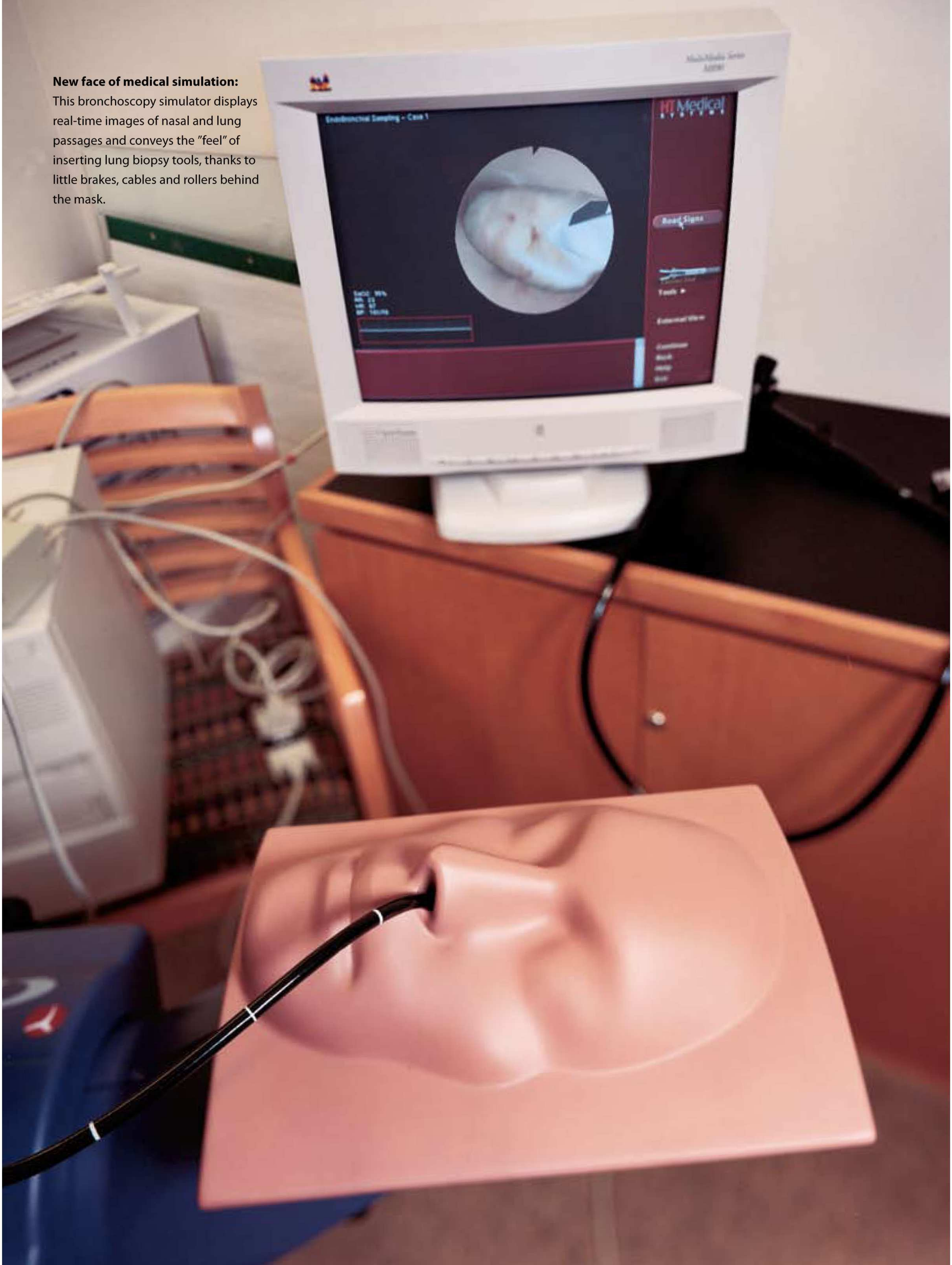
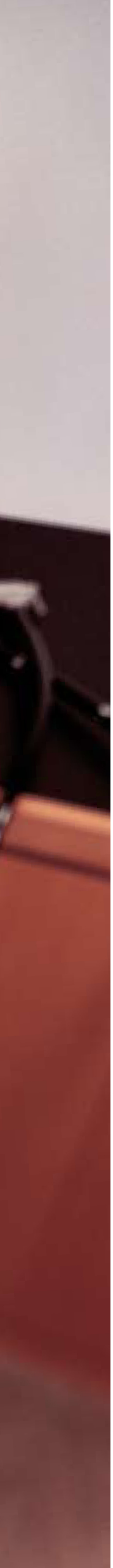


New face of medical simulation: This bronchoscopy simulator displays real-time images of nasal and lung passages and conveys the "feel" of inserting lung biopsy tools, thanks to little brakes, cables and rollers behind the mask.



Helping Doctors Feel Better

As researchers usher the sense of touch into the digital world, medical simulation training gets safer and more palpable.

PHOTOGRAPHS BY BERND AUERS

BY IVAN AMATO

THE PRODUCT DEMONSTRATION room at Immersion Medical in Gaithersburg, MD, is a veritable arcade of medical simulation. There you can find a lineup of electromechanical, sensor-riddled, computerized devices, all coupled to virtual models of the human body. With these gadgets, students can practice the routine task of inserting a catheter into a patient's hand, or more difficult procedures like a colonoscopy or even a lung biopsy. But these simulators don't just provide vivid computerized visual renderings of human innards. They also re-create something equally critical: how all the injecting, cutting, inserting and palpating actually *feel* to the doctor performing them.

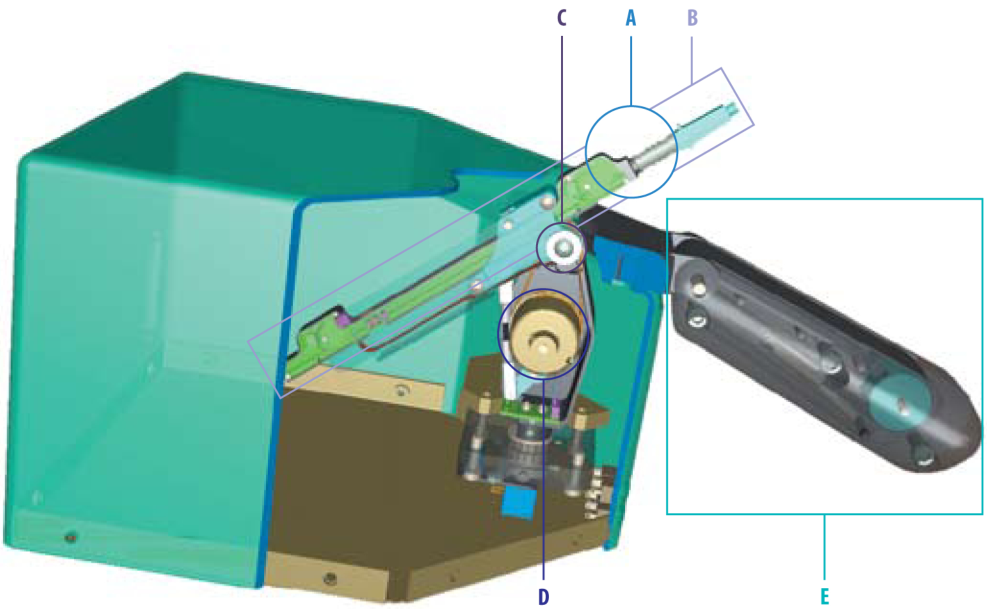
Here and in other corporate and university labs, computer simulation experts—having largely mastered visual displays and digitized sound—are demonstrating an increasing mastery over a third sensory frontier: touch. Their specialty is known as haptics, after the Greek *haptikos*, meaning to grasp or perceive. While the technology is still most widely known as the rudimentary shuddering of a video game joystick, more sophisticated versions are well on their way to enhancing basic medical simulation training.

Future haptic applications may even enable doctors to perform surgery over the Internet. Beyond medicine, haptics has also emerged as a tool for creating "touchable" 3-D models in the virtual world, and for conveying bumps and vibrations on the common computer mouse—you'd "feel" the icons on the screen *(see "Touchy Subjects," p. 70)*. But the technology is having its most palpable impact as an emerging tool for training doctors and nurses without risk to patients. "Haptics is a huge part of providing a realistic [medical] simulation experience," says Gregory Merril, Immersion's 32-year-old founder and self-described chief visionary officer. "When doctors are interacting with patients, a lot of it is the sense of touch."

Boston's Beth Israel Deaconess Medical Center is one of hundreds of hospitals and medical schools that have begun using haptics to train students. The center uses all of Immersion Medical's available haptic simulators, and Mitchell Rabkin, a Beth Israel Deaconess internist and Harvard Medical School professor, believes medical professionals will increasingly rely on haptic simulators in the early

Healing's Virtual Touch

Typical of haptic interfaces, Immersion Medical's "AccuTouch" catheterization training tool conveys a sense of feeling via rollers, cables and brakes as the procedure is simulated on a computer screen.



1: As the user pushes a real catheter/needle end (A), a mechanical sled (B) moves across a roller (C). This action triggers a real-time image of a needle moving toward skin on a computer screen (not shown).

2: As the sled moves forward, Kevlar cables affixed to the roller spin a magnetic particle brake (D), capable of very fine resistances.

3: As the needle "hits" skin and veins on the computer screen, the computer signals the brake to offer resistance at various levels, felt by the user holding the catheter end.

4: The system's handle (E) simulates the feeling of skin and veins—so the trainee can "find" a vein—but provides no haptic feedback.

COURTESY OF IMMERSION MEDICAL

stages of learning new procedures. Although the Immersion devices were only acquired last year and could stand some refinement, he says, "we are encouraged to think that these simulations will indeed have utility"—and may even evolve into objective testing devices for certifying doctors.

So how does this all work? As I stood in Immersion Medical's demo room I wanted to know what it felt like to slide a catheter through skin and into a vein. A company official directed me to their "CathSim" station, where the company's bestselling simulator was displayed. He plugged the business end of a real catheter needle into the simulator's "AccuTouch" haptic interface: a black pivoting connector linked to an aquamarine-colored box approximately the size and shape of an old rotary telephone *(see above)*.

On a computer monitor, a training program allowed me to choose the virtual arm I'd practice on: geriatric, obese, IV drug user. Because I was new to the procedure, I chose something a tad less challenging: the lean arm of a healthy 30-something man. I grasped the catheter with my right hand. With my left, I cradled a handlelike appendage underneath the catheter assembly as though I were holding a patient's arm. Sensors in the interface immediately began recording every move I made with the catheter.

As I nudged the catheter and looked at the monitor, the computer provided both visual and tactile stimuli in real time. The monitor continuously displayed the location of the catheter against the background of my virtual patient's skin. The interface box shunted data about my actions to a computer model of human skin and blood vessels—a model that incorporates how human tissues resist prodding and poking. The model simultaneously projected the feel of the procedure back to my hand via electromechanical components—including Kevlar cables and a magnetic braking system—inside the interface.

The net result of this amalgamation of hardware, software and mechanisms was that the procedure felt intuitively right: easy through the skin, resistance as the needle popped through the blood vessel wall, and a feeling of release as the needle reached the bloodstream. Even my ears were engaged, as my maiden foray into catheterization elicited jarring "ouches" from the computer's speakers: cries of pain from the violated virtual man.

But, hey, I'd done it. Feeling good, I decided to take a stab at something more challenging: pediatrics. But after my third try at easing a thin-gauge catheter into a vein on a newborn baby's virtual forehead, I gave up. My angle was too low. The resistance in the needle told me as much. The virtual baby told me, too, as shrieks rattled the speakers. Maybe I wasn't meant to be a doctor after all.

Merril characterizes the hardware components of his company's simulators as novel uses for existing mechanical and robotic components. With combinations of electromagnetic brakes, motors, cables and other devices, he says it's possible to convey a wide range of tactile sensations. What makes it seem "like you are really sticking the needle in...and that you are feeling a force that corresponds to what you are seeing, is a computer model of the skin," Merril says.

Using critiques from doctors and nurses who have done the real thing many times, software engineers tweak the simulators to improve the fidelity of the haptic sensations. "We know how much force it takes for the surface of the skin to break, and when that happens in the simulator, it tells the machine to let up on the brake," which feels like a sudden reduction of resistance on the ingoing catheter, Merril says. Rabkin adds that

Feeling, but no pain: As the virtual needle touches skin on the screen, a user feels the penetration via the "AccuTouch" interface.


cathSim®
AccuTouch® Interface Device

today's best devices are still a bit jerky, and just short of real time on the visual side.

After wielding a needle, I wanted to try a fancier-looking bronchoscopy simulator, which mimics the device used to inspect the bronchial passages of the lungs. I inserted a straw-thin flexible tube through a nostril of an artificial face staring at the ceiling from a stand. This time, the haptic interface was a free-floating, joystick-like controller—identical to the real medical device—not unlike a bartender's multiple-button, soda-dispensing head. As I snaked the camera- and tool-tipped tube inward, a computer monitor displayed strikingly realistic visual and haptic simulations of the lung's bronchial tree; the simulated airways even convulsed when my "patient" coughed (I forgot to "apply" local anesthetic). I felt particularly doctorly when a menacing mass suddenly became visible. Using a clawlike tool controlled with the haptic interface, I performed a virtual biopsy. A "bloody" spot instantly appeared where I had extracted tissue.

Such were my first encounters with so-called haptic rendering. They undoubtedly won't be the last. These simulators presage haptic things to come in arenas ranging from product design to remotely operated robotic tools, perhaps even hands-on museums where you can rub a virtual Rembrandt. The collective aim of haptics researchers is nothing less than to encode and re-create the world's tactile features with the same breadth and fidelity that has made digital visual and audio rendering so realistic and versatile. To this research community, the tactile surface of the world—real or imagined—is something they can capture, replay, even synthesize from scratch with a combination of computers and handheld gadgetry.

Although there are lots of potential applications on the horizon, medical training appears slated to become the first killer app of haptics. The initial waves of products are already diffusing into medical settings, where students can learn procedures under normal, novel, and unexpected conditions. In the past two years, Immersion Medical says it has shipped approximately 400 medical simulators to hospitals and medical schools. "It's common sense—if that individual can rehearse that circumstance, he will be better able to deal with it when it really happens," says E. James Britt, professor of pulmonary and clinical medicine at the University of Maryland and a consultant to the company.

The CathSim system was launched in 1998, followed by the bronchoscopy simulator in 1999 and a sigmoidoscopy (a similar procedure for inspecting the lower colon) system last year. Immersion Medical—formerly known as HT Medical Systems—remains a wholly owned subsidiary of the San Jose, CA-based computer interface company Immersion, which bought HT Medical last year. Additional product rollouts are planned, including a colonoscopy simulator, which will replicate procedures deeper inside the colon, later this year. All this makes Immersion Medical the leader in commercializing haptics-enhanced medical simulation tools, says Daniel B. Raemer, program coordinator at the Center for Medical Simulation in Boston, MA, which is affiliated with Harvard Medical School.

The company is not alone. Medical Data International, a market analysis firm in Santa Ana, CA, estimates that last year the U.S. market for medical simulation devices—haptic and otherwise—amounted to only $23 million, a figure that is expected to rise substantially in the coming years. Among the other corporate players are MedSim, based in Israel, and Medical Education Technologies, in Sarasota, FL; but these companies' products focus on visual simulations or on medical training mannequins that do not yet include computerized haptics. At Beth Israel Deaconess, residents must demonstrate proficiency with a MedSim device—a non-haptic dummy torso used for ultrasound training—before performing a real intravaginal ultrasound. But with haptics so new, no student is yet required to master any haptics-enhanced device before performing the real procedure, Rabkin says.

And that's largely because the technology still needs a great deal of refinement. The apparent haptic fidelity of these simulators relies on some mental trickery: the visual input helps the brain fill in where the tactile feedback itself falls short; the haptic sensation is still a rough approximation. At the moment, says Bruce Schena, chief technology officer at Immersion, haptics interfaces can convey coarse textural differences, such as the difference between corduroy and smooth cotton. However, it's not possible to distinguish subtler differences between, say, cotton and polyester. When it comes to haptic fidelity, "we are in the days of eight-bit color," or roughly at the cartoon level, Schena says.

Haptic rendering has taken longer to come online than visual rendering because it is a vastly more difficult problem, says

Dr. Feelgood: Dr. Mitchell Rabkin of Harvard Medical School explains virtual catheterization at Beth Israel Deaconess Medical Center.

Touchy Subjects: From Digital Clay to the "nanoManipulator"

You can't take more than a few steps in the world of haptics research without bumping into the Phantom. While medical applications are haptics' primary commercial drivers at the moment, the Phantom—a haptic interface looking somewhat like a black retractable table lamp with a thimble or stylus at the end—is feeling its way through applications ranging from a 3-D sculpting device to a tool for a virtual "hands-on museum."

Mechanical devices inside the interface convey the "feel" of a computer image via the retractable arm, which is held by the user. Since inventing it in the early 1990s while a graduate student in MIT's Artificial Intelligence lab, Thomas Massie, founder and chief technology officer of SensAble Technologies in Woburn, MA, has churned out a continuously improving line of Phantoms and accompanying software for hundreds of customers. To Massie, a pioneer haptics gadgeteer, the technology's future lies in the realm of computer-aided design and manufacturing as a tool for "sculpting" virtual objects rendered in 3-D.

SensAble's FreeForm technology enables users to work with "digital clay" on the screen, while feeling some semblance of the chipping and scraping through the Phantom. Massie sees visually and haptically rendered digital prototypes as eliminating the need for labor-intensive hand-built models. "You can scale [the digital model] up or down in size, archive it, you can mirror it, so you don't have to design both halves of a car or both soles of a pair of shoes," he says. The design can be shared over networks and the Internet and fed directly to computer-aided manufacturing systems or rapid-prototyping machines.

Among the larger users of FreeForm so far are Motorola, Hasbro, Adidas and Honda, who have used it to design tennis shoes, golf clubs, wireless device housings and action figures. And in one of Phantom's more Star-Trekky applications, researchers at the University of North Carolina connected a Phantom to an atomic force microscope so users can "feel" the molecular landscapes of surfaces. The result: the nanoManipulator.

Others are adapting the Phantom interface in novel ways. Social scientist Margaret McLaughlin, of the Integrated Media Systems Center at the University of Southern California, has begun using it to advance ideas like "hands-on" virtual museums. "The first thing you learn when you start going to museums is 'Don't touch anything,'" McLaughlin says. She is aiming to make it possible to, say, reach out and caress a virtual version of the Hope Diamond. As a pilot project, McLaughlin and coworkers scanned a collection of ornamental teapots, including a wicker one, at USC's Fisher Gallery so a computer monitor could display them in 3-D and a Phantom user could "feel" them. However, today's state of the Phantom art allows touching with only one stylus—meaning one finger.

In a more hands-on idea, the USC researchers are using the Phantom and another haptic interface, the CyberGrasp, to move humanity closer to the day when "mutual touching" will become possible over the Internet. The CyberGrasp—made by Palo Alto, CA-based Virtual Technologies—fits over the hand like a glove and can transmit a full-hand sensation via a network of artificial tendons. On one end of an Internet connection, a Phantom user strokes a virtual image of a CyberGrasp glove depicted on his computer screen; on the other, his partner, wearing an actual CyberGrasp glove, feels the sensation. (From there it doesn't take much to envision the arrival of what is jokingly termed "teledildonics," or sexual contact over the Internet.)

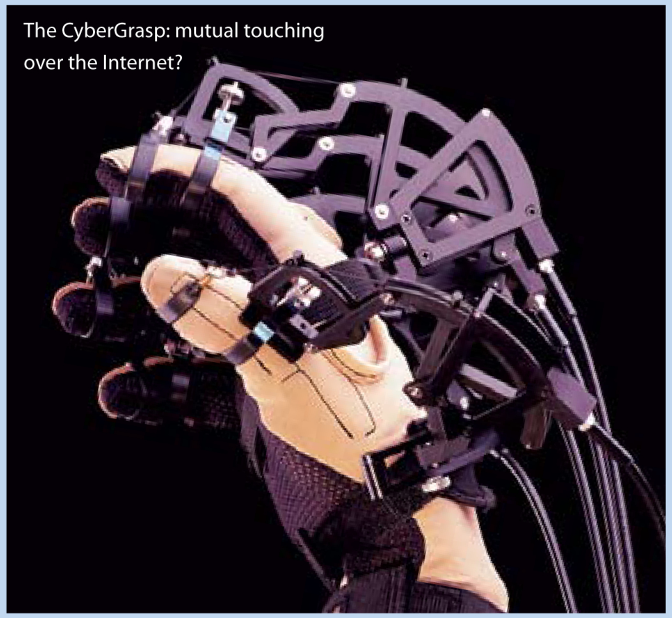
McLaughlin believes "mutual touch" haptics is ideal for effective collaborative design. She suspects it will even become possible to capture and play back haptic experiences in a new form of master-apprentice relationship, which would allow in-the-hands knowledge of artists and artisans to become digitized and preserved for future students.

A more pedestrian bid to bring haptic technology to the masses is Logitech's new $59.95 iFeel MouseMan mouse, which relies on software licensed from San Jose, CA-based Immersion. The mouse allows users to "feel" on-screen buttons, menus and scroll bars. Web site developers can also embed haptic information in their sites' source code. A person wielding an iFeel mouse would feel any tactile sensations linked to features on the site.

The iFeel mouse includes a special motor, known as an Inertial Harmonic Drive. Meshed gears, including a flexible one, generate vibration and motion as a result of a mismatch in the tooth-number of the gears and an attached small mass. First invented in the 1950s for aerospace applications, the Inertial Harmonic Drive inside the new mouse generates tactile sensations as it accelerates, decelerates, stops and starts. Says Bruce Schena, Immersion's chief technology officer, "Now Window borders feel like Window borders, and clicks feel like clicks." **—Ivan Amato**

Of mice and modeling: Haptic interfaces range from a vibrating mouse (left) to a glove allowing whole-hand "touching" of virtual objects (center). The groundbreaking Phantom (right) puts "feel" in 3-D model making.


Haptics for $59.95: the iFeel MouseMan


The CyberGrasp: mutual touching over the Internet?


The Phantom: digital sculpting

physicist and haptics engineer Ralph Hollis of the Robotics Institute at Carnegie Mellon University in Pittsburgh. Rendering visual images is a one-way street. "Eyes take in photons but don't shoot them out," says Hollis, who designs haptic devices for controlling factory tools and robotic machinery. But haptics devices are two-way. "A hand manipulates, but there is force feedback too. So any kind of haptic device that we use to interface with the computer must…take input from users as well as deliver output through the same mechanism."

In addition to this two-way problem, designers face a major computational challenge: simulating feeling is far more demanding than simulating seeing. Film projected at 24 frames per second creates the illusion of a continuous moving image; but, says Hollis, "You might need 1000 frames to fool the sense of touch." This goes a long way toward explaining why haptics is just now building genuine momentum. Not until the past few years did computing power become cheap enough for Immersion Medical to reduce Haptics product prices below $10,000.

Even as haptics-enhanced training devices spread within the medical community, some physicians are eyeing another haptic frontier: telesurgery. They envision surgery—complete with the sense of feel—transacted over the Internet or even via datalinks to far-flung places like the International Space Station. This would be particularly helpful in the area of minimally invasive surgery, including the so-called laparoscopic procedures. In such procedures, doctors snake tiny cameras, scoops and knives into the body through thin tubes. The doctors operate the tools with mechanical controllers and watch the action on a video screen.

Such procedures have been great for patients, who experience smaller wounds, fewer infections and quicker recoveries. But they place new demands on doctors. By not opening the abdomen, says surgery professor Richard M. Satava of the Yale University Medical School, the surgeon suffers "a loss of 3-D vision, dexterity and the sense of touch." As medicine moves toward more laparoscopic procedures—whether performed telesurgically or on site—haptics-based simulators can help doctors overcome those sensory deficits.

Haptics also promises to push the frontiers of robotic surgery. For example, Satava says it probably will become possible for surgeons to plan minimally invasive operations—using feedback from haptic renderings of the procedure—then allow robots to do the actual cutting. Some advances in this direction have already occurred. Computer Motion, based in Santa Barbara, CA, has sold about 40 of its ZEUS Robotic Surgical Systems, in which doctors control robots that wield three tool-tipped arms inserted into the patient. One of those robotic arms transmits forces experienced by the tool back to the human surgeon's hand. One chief competitor: Intuitive Surgical of Mountain View, CA, whose flagship product, the da Vinci Surgical System, offers a similar combination of computers and robotics *(see "RoboSurgeons,"* TR *November/December 2000).*

This future era of haptics-enhanced telesurgery and robotic surgery, Satava says, will require new models of human beings that include haptic parameters such as the resistance that various tissues offer when a knife or needle goes through them. A good place to start, he says, would be to expand on the National Library of Medicine's Visible Human Project, launched in the mid-1990s. Male and female cadavers were sectioned at intervals of 1 millimeter and .33 millimeters, respectively. Each section was imaged by CAT scan, photography and other tools, then digitized and integrated into an enormous visual and informational database. "Now we need to add all the properties for the sense of touch," Satava says. "That way, when a doctor gets a CT scan, he would be able to use a haptic interface to feel the 3-D model displayed on a computer screen."

And Satava and Merril have an even more exotic vision for robotic medical haptics. A master surgeon could haptically record an intricate brain operation on a virtual rendering of a patient. A novice surgeon could use the master's recording to rehearse the procedure, complete with tactile feedback personalized for that patient. Add robotics to this scenario, and it might become possible for a surgeon to perform an operation on himself, by doing it first in the virtual world, then unleashing a robot to "play back" the real thing. But that's a long way off. What's clear, Raemer says, is that today's applications of haptics technology "are just barely scratching the surface." ◊

TECHNOLOGY REVIEW April 2001

Spare part: Anthony Atala holds a full-sized, functional bladder—built right in his lab.

WHAT IF GETTING A REPLACEMENT FOR A FAILING HEART OR LIVER WERE AS EASY AS BUYING A NEW MUFFLER? RECENT ADVANCES IN A FIELD KNOWN AS TISSUE ENGINEERING COULD MAKE IT HAPPEN.

The Human Body Shop

BY DOUG GARR

PHOTOGRAPHS BY BETH PERKINS

IT'S A DECADE FROM NOW, AND AN ELDERLY MAN GETS THE GRIM NEWS THAT HIS heart is rapidly decaying and that the left ventricle—the chamber that squeezes blood out to the body—needs to be replaced. His physician takes a biopsy of the heart cells that are still healthy and ships the tissue to a lab that is really an organ factory. There, workers use the patient's own cells and special polymers to fashion and grow a replacement part—certified by the original manufacturer. In three months, the new ventricle is frozen, packaged and sent to the hospital, where the patient undergoes a standard surgical procedure: the insertion of a living implant created from his own tissue. The surgery saves his life.

Not long ago, the notion of designing and growing living replacement body parts—a process now known as tissue engineering—seemed pure fantasy. But researchers in biotechnology are confident that the day will come when scenarios like the one above will be real and commonplace, thanks to advances made in the last decade in "biomaterials" that are compatible with living cells and the cultivation of new tissue, and to a far better understanding of how cells actually behave. The only question is, when? Some predict that within 20 years, possibly sooner, replacement ventricles, bladders, and the like will be readily available. For complex organs like lungs, though, it could take until mid-century.

A RUN ON ORGANS

For ill patients, breakthroughs in tissue-engineered organs can't come soon enough. The shortage of donor organs is infamous. In 1999 (the most recent year for which complete data are available) there were more than 72,000 people in the United States alone on transplant waiting lists, according to statistics from the United Network for Organ Sharing. By year's end, over 6,100 people had died waiting. Dozens of groups in industry and academia are hoping to prevent those deaths, working on techniques for fashioning new organs out of cells from embryos, cadavers or patients themselves, combined with special biomaterials. Most current work in the commercial realm focuses on tissues, valves and other components of organs *(see "Tissue Engineering in Industry," p. 76)*. Already, there are a handful of tissue-engineered products on the market—skin, bone, and cartilage implants and patches—the first successes in a young field.

Michael Ehrenreich, president of Techvest, a New York-based investment company that closely follows the biotech sector, feels such achievements are only an indication of what's to come, and he is blunt about where tissue engineering is now. "Skin. Big deal. It's a proof of concept," says Ehrenreich. "At the end of the day, many of us are going to die from some sort of organ failure. That's what's going to drive this market. And nobody's really tackled a vascularized organ yet."

Ehrenreich has touched on one of the more vexing problems facing tissue engineers: most organs need their own vasculature, or network of blood vessels, to get the nutrients they need to survive and to perform their intended functions. So before researchers can build a full-sized organ, such as a liver, say, or a set of lungs, they must learn to manufacture blood vessels.

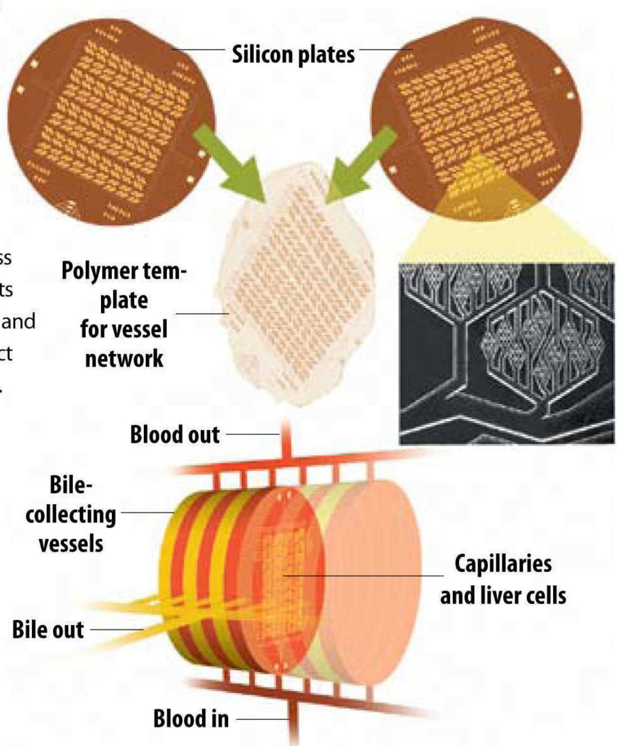
BLOODLINES

Important progress on that front came two years ago, when MIT biomedical

Building a Liver in Layers

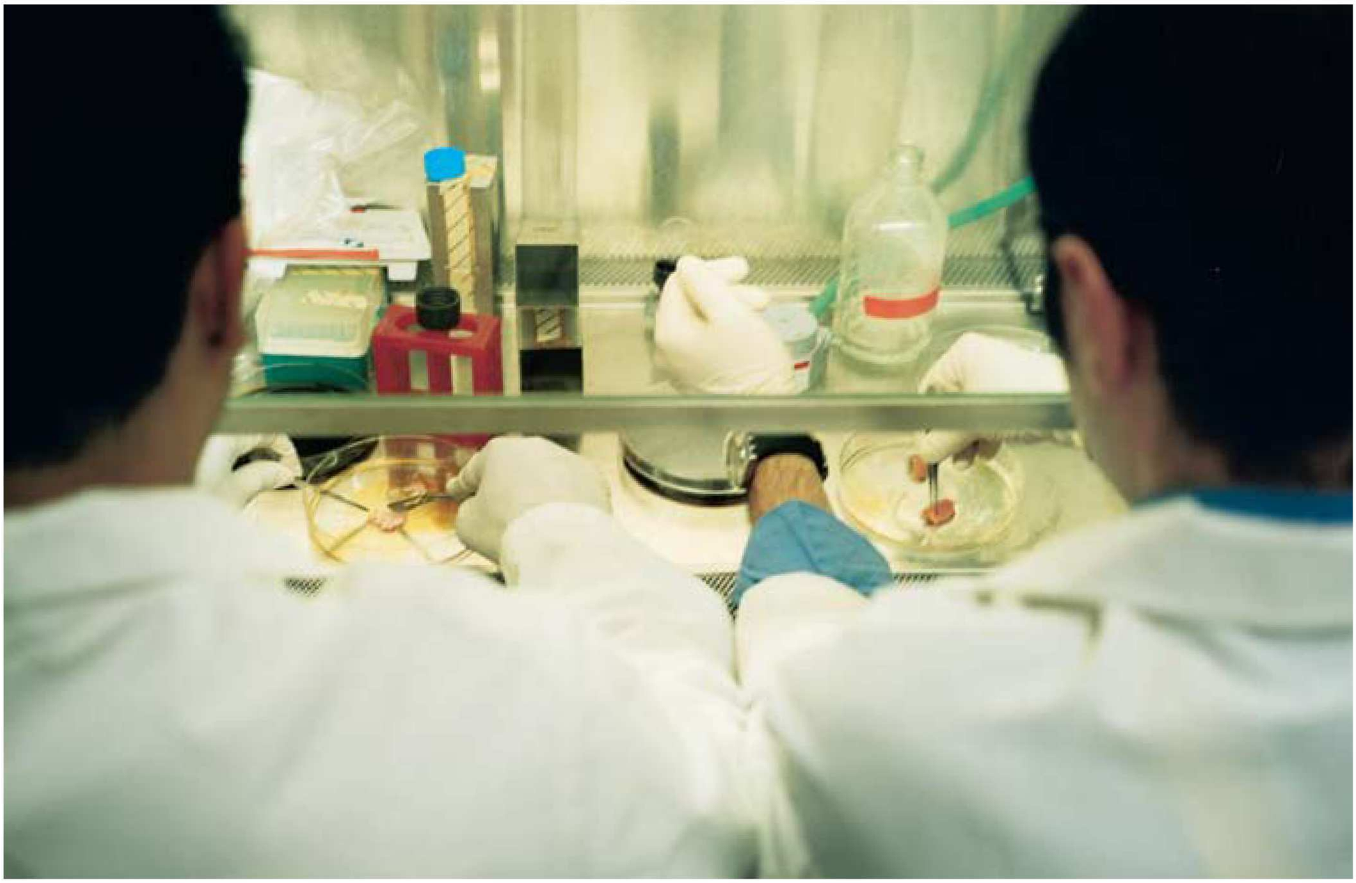
Researchers might begin by etching networks of capillary-like grooves on palm-sized silicon plates—forming molds for a biodegradable polymer. Two casts, lifted from the molds and sandwiched together, would create a three-dimensional template for interconnected vessels.

Next, the inside surfaces of the templates would be seeded with special lining cells, and liver cells would be added to the outside. That way, blood flowing through the new capillaries could exchange nutrients and wastes with the liver cells across the porous polymer. Other casts would receive lining cells only, and would serve as vessels to collect bile produced by the liver cells.



A human-sized artificial liver might include several thousand stacked layers of capillaries, liver cells and bile-collecting vessels. Implanted in the abdomen, the device could receive blood from the body and filter it through the capillaries. The adjacent liver cells would cleanse the blood of toxins and secrete bile into collecting vessels.

BETSY HAYES; SOURCE: ELI WEINBERG



Smaller donations: To engineer an organ, researchers start with just a small tissue sample. Eventually, patients may be able to be their own donors.

engineers Robert Langer and Laura Niklason (now at Duke University Medical Center) grew entire blood vessels from a few cells collected from pigs. Niklason, who led the effort and did much of the work during a stint in Langer's lab, started by taking small biopsies from the carotid arteries of six-month-old miniature swine. She isolated smooth muscle cells from each tissue sample and used those cells to seed the outer surface of a tubular scaffold built of a biodegradable polymer used in sutures. Next, Niklason cultured each new vessel in its own special growth chamber called a bioreactor. Bioreactors are standard in tissue engineering, but in this case there was a twist.

As Langer explains, "What we did is we set up these little pumps that beat like a heart and hooked them up to the artificial blood vessels." The researchers found that the pulsation encouraged the muscle cells to migrate inward, enveloping microscopic fragments of the polymer, and ultimately made the blood vessels much stronger. After growing the vessels in the pulsing environment for several weeks, they added endothelial cells—the thin, flat cells that line the inside of many tissues, including blood vessels—to their inner surfaces, and grew them for a few more days.

"That single change totally changed everything," says Langer. "We were actually able to make blood vessels that looked like real vessels." They functioned like real blood vessels too, staying open and clot-free for several weeks when the researchers grafted them into large arteries in the pigs' legs. "The key to getting this to work was to mimic what the body did" by growing the vessels in an environment that pulsed just as a real circulatory system does, says Langer.

While new, artery-sized blood vessels could be a godsend for surgeries like heart bypass, building more complex organs will also require the smallest of blood vessels: capillaries. And since that means tissue engineering on the scale of microns, or millionths of a meter, it's an even greater challenge. To meet that challenge, pediatric surgeon and prominent tissue engineer Joseph Vacanti of Massachusetts General Hospital enlisted the help of colleagues at Draper Laboratory in Cambridge, MA. Vacanti was convinced that the techniques used to etch computer chips could also help build capillaries.

Physicist Jeff Borenstein, who directs Draper's microfabrication program, was encouraged to learn that the smallest human capillary was 10 microns in diameter; he was accustomed to working with computer-chip features about 10 times smaller. "We can draw that with a dull pencil," Borenstein says. "A capillary is like falling off a log for us." The team etched interconnected networks of capillary-like grooves into palm-sized wafers of silicon or Pyrex. In initial experiments, they seeded the wafers with endothelial cells from a rat. The cells grew to line the etched grooves; two cell layers grown this way and sandwiched together formed new vessels that could carry fluid *(see "Blood from a Chip,"* TR *May/June 2000).*

In ongoing work, the researchers are instead using the etched wafers as molds in which they cast a biodegradable polymer. The polymer casts can be pulled out of the molds and sandwiched together to form a scaffold for full three-dimensional vessels; then the scaffold can be seeded with endothelial cells. Of course, just one cast's worth of capillaries would not be enough to supply blood to an entire

Assembly line: In Anthony Atala's lab, organ production starts with polymer scaffolds (left). In the foreground are kidney-tissue scaffolds; in the background is one for a branching blood vessel. Next, researchers harvest cells from donor tissue (right) and use them to seed the scaffolds.

organ. Borenstein once calculated the area of capillary networks needed to support a liver. "It's a pretty large area," he says. "It was something like a small conference-room table for a rat, and a quarter of a football field for an adult human. You can't come up with wafers that are [30 meters] in diameter." So by combining thousands of layers of capillary networks together with liver cells, the researchers hope to create the basic structure for an artificial liver *(see "Building a Liver in Layers," p. 74)*.

BEAGLE BLADDERS AND HUMAN HEARTS

Even without the technology to build extensive vascular systems, one tissue-engineered organ has made it almost all the way to human trials: the bladder. Anthony Atala, a urologist and director of tissue engineering at Children's Hospital, Boston, decided to try to build a bladder in part because it seemed like the easiest organ to begin with. In landmark work done in the late 1990s, Atala's team built new bladders for six beagles. The researchers started by taking a one-centimeter-square biopsy from each dog's natural bladder, isolating the lining cells and the muscle cells from the biopsy, and culturing each cell type separately.

After a month, Atala's team had grown enough cells—300 million of each type—to construct an artificial bladder. They used the muscle cells to sheathe the outside of a bladder-shaped polymer scaffold, and the lining cells to cover the inside. The researchers implanted each new bladder into a dog after removing the dog's own bladder. The researchers discovered that not only did blood vessels from the surrounding tissue grow into the tissue-engineered bladder and keep its tissues healthy, but the dogs also had almost as much bladder capacity as dogs with original equipment.

The early work went so well that Atala and Cambridge, MA-based Curis hope to begin the first tests of the new bladder in humans sometime this year. Still, Atala is realistic about what he's already accomplished. For one thing, he has not yet answered the question of how long a bioengineered bladder will last. "With the bladder, it's going to be several years until we know what the long-term results will be," he explains. "We certainly have a good history with skin. Twenty years down the road we know it's fine. With cartilage in the knee, we have a four- or five-year history from the time it was first placed in patients." But with the bladder, Atala says, "We just don't know."

In the meanwhile, Atala's lab has begun to tackle the kidney and has already built small kidneylike units capable of producing urine. Still, given that the kidney is a highly complex structure that includes as many as 20 different types of cells, researchers have to clear many technical hurdles before making full-sized organs for the nearly 48,000 people waiting on kidney transplant lists in the United States alone.

Tissue-engineering a heart will also be a formidable task, but there are a couple of reasons to believe concrete steps in that direction will be made in the not-too-distant future. For one thing, the heart comprises fewer than 10 different cell types. Perhaps even more important, there are two large research consortia targeting the organ. One is the LIFE initiative (for "Living Implants from Engineering"), begun in 1998 and coordinated by the University of Toronto's Michael Sefton, with the help of a steering committee that includes Massachu-

Tissue Engineering in Industry

Here are just a few of the biotech firms trying to build new tissues and organs

COMPANY	LOCATION	PRODUCTS IN THE PIPELINE
Advanced Tissue Sciences	La Jolla, CA	Skin (TransCyte, Dermagraft); cartilage, ligaments and tendons; blood vessels and heart valves
Genzyme Biosurgery	Cambridge, MA	Cartilage cells (Carticel); cartilage graft (Carticel II)
CryoLife	Kennesaw, GA	Heart valves and blood vessels; ligaments
Curis	Cambridge, MA	Cartilage gel to prevent urinary reflux (Chondrogel); bladder
LifeCell	Branchburg, NJ	Skin (AlloDerm); blood vessels; ligaments and tendons
Organogenesis	Canton, MA	Skin (Apligraf, Vitrix); blood vessels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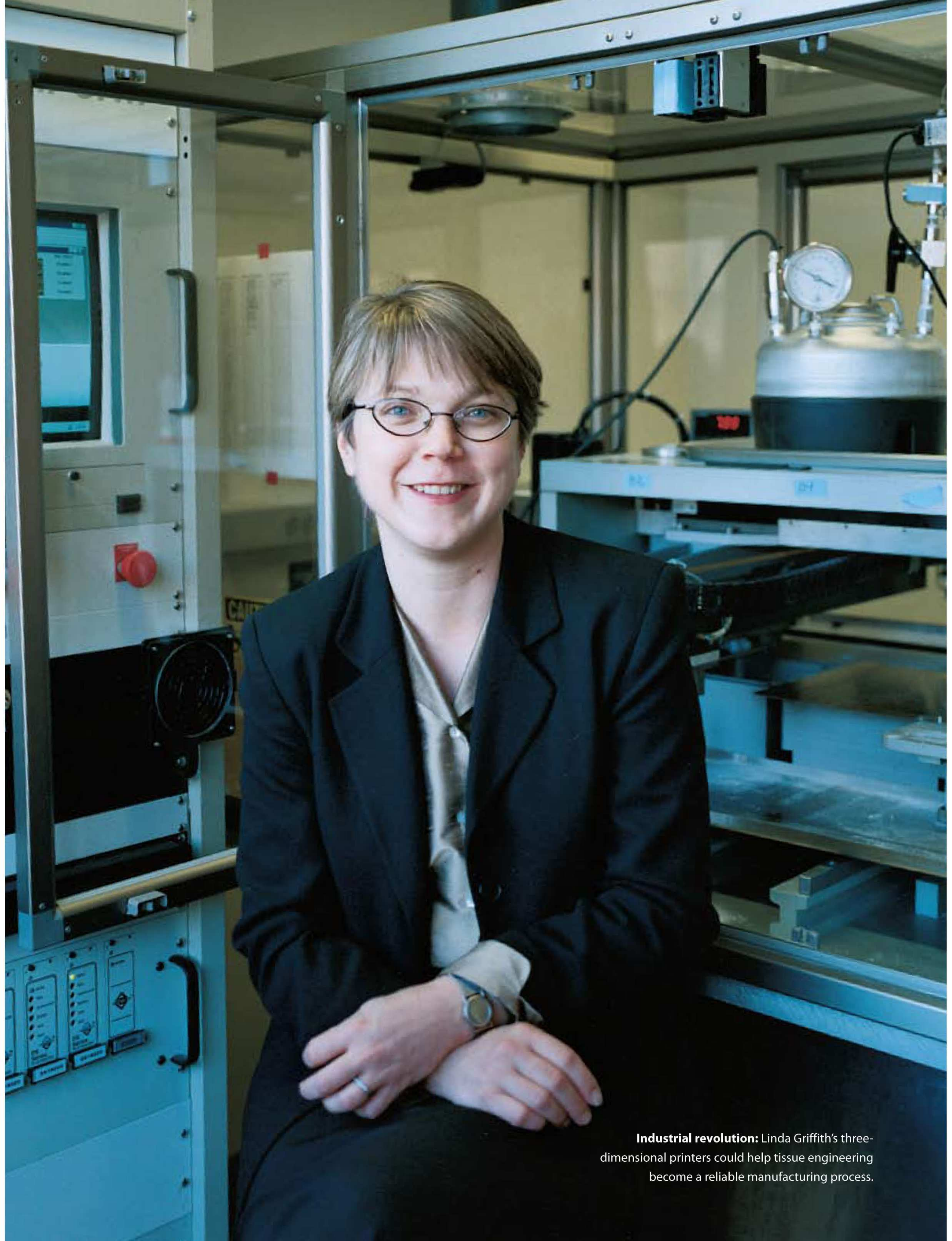

Industrial revolution: Linda Griffith's three-dimensional printers could help tissue engineering become a reliable manufacturing process.

Powder power: Griffith's scaffold printer first rolls out a thin layer of polymer powder (top and bottom left). An inkjet printer head distributes liquid binder to harden the right areas of that layer. By repeating the process many times, the machine can build a variety of shapes (above).

setts General Hospital's Vacanti and MIT's Langer. The initiative has marshaled 60 academic and government researchers from North America, Europe and Japan to work on the body's critical pump. Says Sefton, "If we can solve the heart, then the other organs will follow."

Sefton readily admits that a project as enormous as building the heart is, on the face of it, ridiculous. Still, he believes that by breaking the job down into component tasks—isolating human cardiac muscle cells, say, or building flexible scaffolds to support those cells—a consortium of researchers will be able to make it happen.

That model is also being tested, Sefton says, in a university/industry collaboration led by the University of Washington. Financed by a $10 million grant from the National Institutes of Health and including more than 40 researchers, the University of Washington project has broken its undertaking into a series of goals. The first is to generate a tissue-engineered patch that can be grafted onto a damaged heart. Longer term, the researchers hope to build implantable left ventricles, a goal Sefton sees as a "mini-moonshot" that could be achieved within the decade. But a fully functional bioengineered heart, Sefton says, will likely cost billions of dollars—and neither the LIFE initiative nor the University of Washington's has raised that kind of money yet.

STRAIGHT FROM THE FACTORY

Ultimately, any method for building new human organs will have to win approval from the U.S. Food and Drug Administration. And that means organ builders will need a standardized, reproducible manufacturing process, says MIT bioengineer Linda Griffith. To achieve that goal, Griffith and her colleagues have turned to a device invented by MIT engineer Emanuel Sachs and used for rapid prototyping and the manufacture of a variety of parts and tools: a three-dimensional powder printer, or 3DP machine.

The machine builds up complex shapes layer by layer, based on a computer file capable of depicting the object as a series of horizontal slices. A roller pushes a thin layer of powder across a flat base plate resting on top of a piston. Next, an inkjet printer head distributes a glue, or binder, to solidify the powder only where the blueprint for that slice calls for solid material. The piston then ratchets the plate down by the thickness of the layer, and the process begins again. When all the layers have been printed, the new object can be removed from the machine, and the excess powder falls away.

By adapting the printer to use polymer powders, multiple print heads and special binders, Griffith and her collaborators created a tool capable of mass-producing polymer scaffolds for new tissues and organs. Not only does the printer allow the researchers to control a scaffold's shape with great precision, it also allows them to build in chemical modifications to the structure's surface that help tell different types of cells exactly where and how they should grow.

It's just that sort of fine control that may help tissue engineers conquer even the most complicated organs. Indeed, Griffith is now—along with Vacanti and Princeton, NJ-based Therics—working out ways to manufacture livers and other organs with three-dimensional printing. Griffith already knows a great deal about growing liver tissue; she worked on the details while leading an effort to develop a liver-cell-based biological-weapon detector for the U.S. Defense Advanced Research Projects Agency. The hope is that scientific knowledge, combined with three-dimensional-printing technology, will make building a liver for implantation possible.

If everything pans out as Griffith, Vacanti and their colleagues hope, manufacturing machines could someday hum in FDA-certified organ factories. It's too soon to know if those factories will churn out entire organs on site, or if they'll instead produce and ship elaborate scaffold structures on which doctors will grow patients' own cells, right in the hospital. But either approach, if successful, promises one thing: an end to transplant waiting lists. ◊

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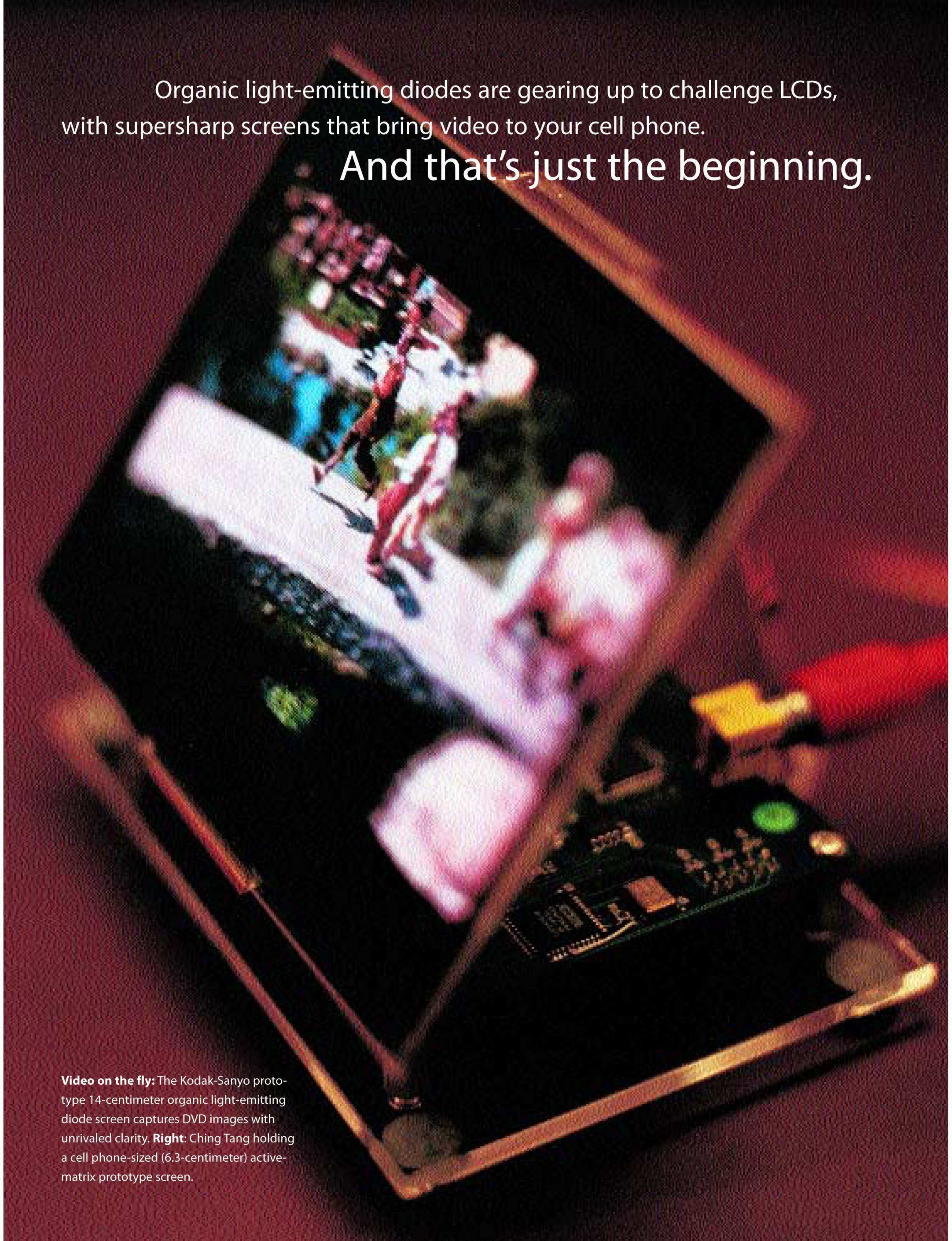
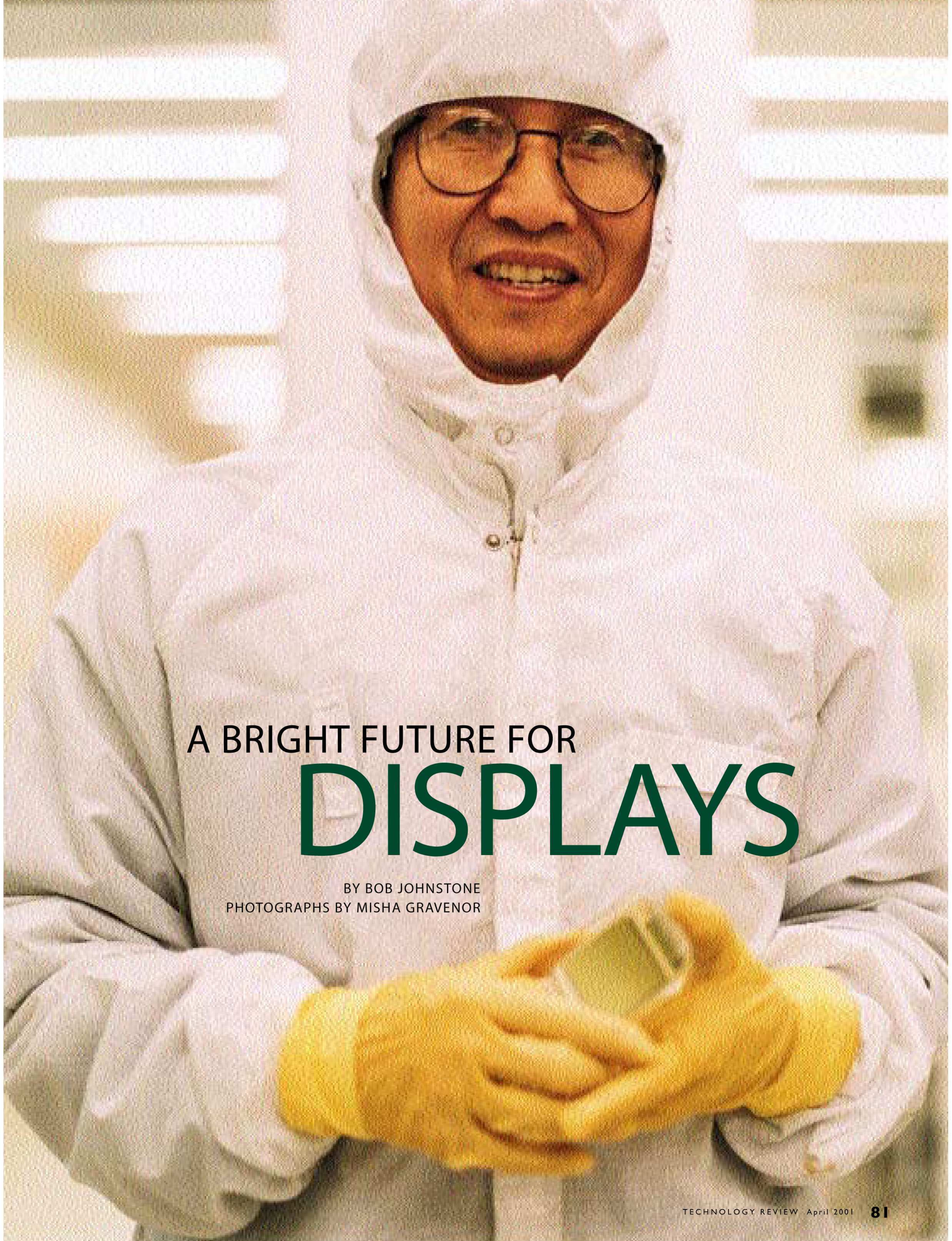
Organic light-emitting diodes are gearing up to challenge LCDs, with supersharp screens that bring video to your cell phone.

And that's just the beginning.



Video on the fly: The Kodak-Sanyo prototype 14-centimeter organic light-emitting diode screen captures DVD images with unrivaled clarity. **Right**: Ching Tang holding a cell phone-sized (6.3-centimeter) active-matrix prototype screen.



A BRIGHT FUTURE FOR DISPLAYS

BY BOB JOHNSTONE

PHOTOGRAPHS BY MISHA GRAVENOR

Every year, thousands of tourists flock to the California coastal city of Long Beach, the last resting place of the ocean liner Queen Mary—a notable showcase of what was once state-of-the-art technology. But for a select group of visitors last May, the city's main attraction was not a memento of the past but a technology of the future: a dime-thin sheet of glass 14 centimeters along the diagonal whose unparalleled ability to exhibit ultrabright colors and process high-clarity video images holds the potential to have far greater impact on the world than any single ship, no matter how splendid.

Based on a technology called organic light-emitting diodes, the prototype screen was unveiled by Eastman Kodak and Sanyo Electric at the annual conference of the Society of Information Display, the industry's top professional group. As the screen was put through its paces, running images from video cassette, DVD and digital tape, even grizzled veterans of the flat-panel industry who packed into the Kodak booth came away goggle-eyed. Little wonder. Organic light-emitting diodes are shaping up as a superdisplay: brighter, thinner, lighter and faster than liquid crystal displays. They also take less power to run, offer higher contrast, look equally bright from all angles and have the potential to be much cheaper to manufacture than their conventional counterparts.

These advantages, especially the ability to handle video, give the upstart technology the inside track to become the screen of choice for the coming third generation of mobile phones. About to debut in Japan, the third-generation standard seeks to spur the production of phones that are aimed at eyes as well as ears, by giving them the ability to handle high-speed video over the Internet. These wireless Web phones are expected to quickly become a multibillion-dollar global business. But that may be only the start for organic light-emitting diodes, which are threatening to challenge the 30-year hegemony of liquid crystal displays in a broad range of portable electronics.

This promise has fired the imaginations of scientists and engineers and spurred a worldwide race to develop the technology that pits startups against heavyweights such as Kodak and Sanyo. Difficult problems remain to be solved before the promise can be realized. But the potential is too great for some savvy technology companies to ignore. Notes Dalen Keys, chief technology officer of DuPont Displays, the chemical giant's spinoff that is out to win a big share of this emerging market, "We are trying to achieve a complete change of the paradigm of what is a display, and the cost of the display."

A STRANGE BLUE GLOW

If ever a technology has begged to be disrupted, it is liquid crystal displays. Invented in 1963 and originally envisioned as a slimmed-down replacement for bulky cathode-ray tubes or as screens for wall-mounted televisions—a use never realized due to problems scaling up to large surfaces—liquid crystal displays have instead become the standard for everything from watches to laptop computers.

In spite of its spread, however, this ubiquitous technology has an Achilles' heel: the screens are hard to make and therefore expensive—especially when it comes to high-end versions used in color displays. Indeed, they account for as much as a third of the cost of a laptop, and the failure to bring down the price of portables as dramatically as the price of personal computers has been due largely to the inability to simplify display-screen production.

Perhaps the remarkable thing about liquid crystal displays is not that they are so expensive but that, given their technological complexity, they are affordable at all. The core of the screen is a sandwich of two flat sheets of glass a few microns apart, with the liquid crystals that form the display medium poured in between. Since the crystals themselves cannot produce light, it's necessary to provide a source—a backlight. A diffuser is then needed to distribute the light evenly across the crystals, as well as front-and-back polarizers to orient the light. And that's just for monochromatic screens. Full-color displays also require expensive red/green/blue filters made of dichromated gelatin—fish glue. To make things fast and bright for, say, a laptop requires another pricey addition: an active-matrix backplane that puts a thin-film transistor behind every pixel. Finally, to manufacture this Byzantine monster takes a super-clean factory that won't leave much change out of a billion-dollar bill.

The result is that for the dozen or so firms, mostly Japanese, that have overcome these obstacles to produce active-matrix liquid crystal displays—only to see them become a commodity item, with wafer-thin margins to match—victory has often been Pyrrhic.

Into this chasm of opportunity, with the potential for cheaper but higher-margin and more versatile displays made of common materials like the dyes used in photocopying and photographic paper, come organic light-emitting diodes. Their story begins in 1979, with a scene straight out of a low-budget sci-fi movie. That's when Ching Tang, a Hong Kong-born chemist at Kodak's research laboratories in Rochester, NY, noticed that one of the organic solar cells he was working on was giving off…well, a strange, blue glow. Curiosity aroused, the Kodak scientist launched a long investigation into this phenomenon, known as "organic electroluminescence." His seminal work, reported in *Applied Physics Letters* in 1987, showed that organic materials were efficient converters of electricity into light that could be switched on and off quickly—especially crucial for showing video, where images are updated 50 or 60 times a second and get blurred if the screen can't keep up. Furthermore, Tang noted, these effects could be obtained with low voltage. In short, organic light-emitting diodes had

Organic light-emitting diodes represent the only **display technology poised to** meet third-generation mobile phone standards.

all the makings of a sensational display technology.

Another breakthrough occurred a year later, when Jeremy Burroughes, a doctoral student at the University of Cambridge's famous Cavendish Laboratory, showed that electroluminescence was characteristic not just of the small molecules studied by Tang but also of far larger polymer molecules *(see "Displaying a Winning Glow,"* TR *January/February 1999)*. This was important because it's much easier in principle to make displays out of polymers than out of small molecules. The smaller materials must be vaporized in a vacuum, then patterned through a perforated metal foil or shadow mask—a costly and delicate process. At least for monochrome displays, however, polymers can be deposited by inexpensive "spin-coating," in which they are simply squirted at a rotating target to achieve a uniform surface.

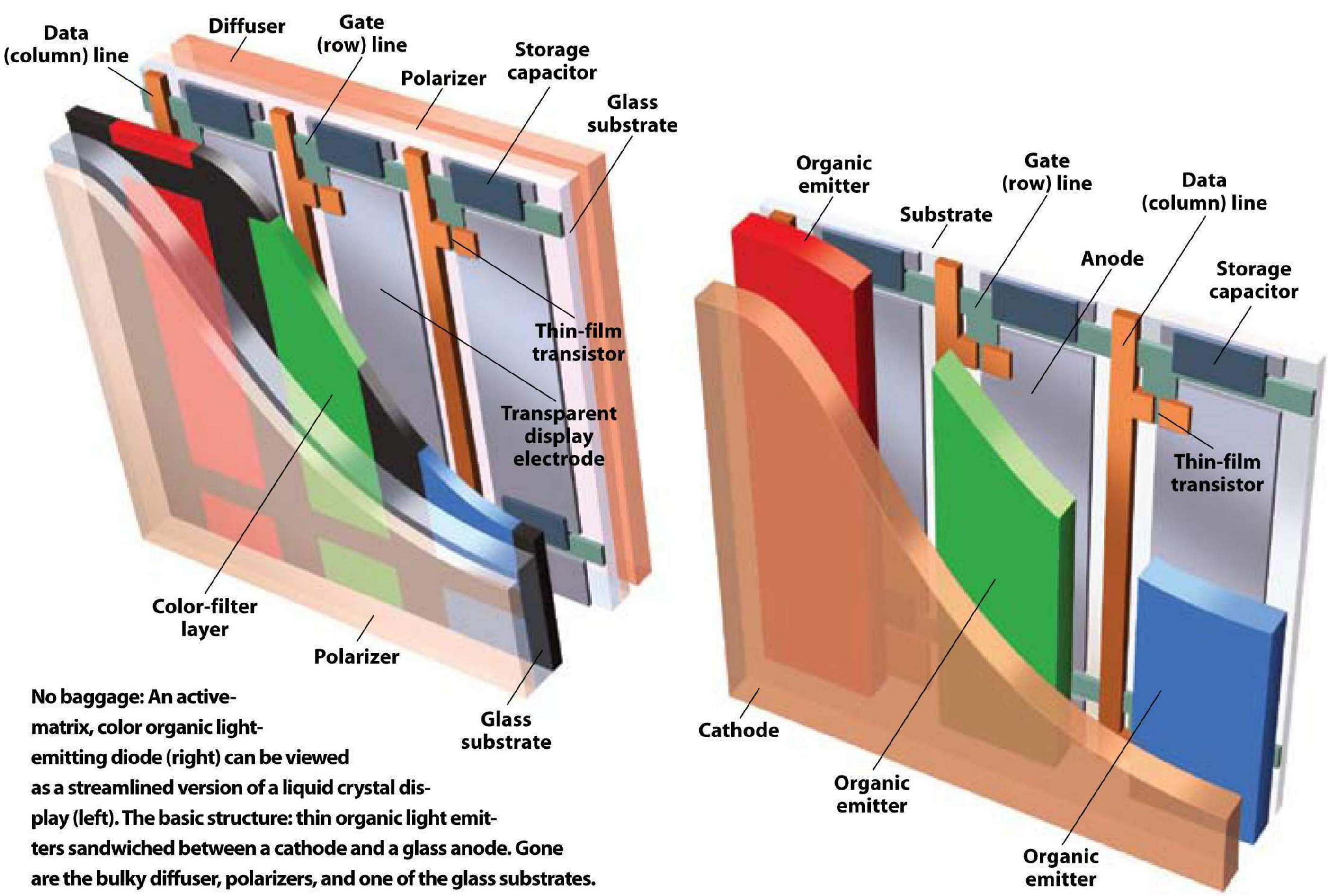
This finding helped catapult the technology into prime time. Burroughes and his professor, Richard Friend, formed Cambridge Display Technology, which established itself alongside Kodak as a key player in the race to commercialize organic light-emitting diodes. Although these pioneers had the field to themselves briefly, they're not alone anymore. David E. Mentley, a senior vice president with San Jose, CA-based market research firm Stanford Resources, estimates that some 90 other companies have since joined the fray. These include giants Philips, DuPont and NEC, as well as startups eMagin and Uniax, a Santa Barbara, CA, firm founded on technology from Nobel laureate chemist Alan Heeger (DuPont bought the company last year). Some license the Cambridge polymer technology; some follow Kodak's small-molecule lead; some pursue their own variants. Whatever the strategy, a savage battle to commercialize organic light-emitting diodes is underway *(see "Global Race for a Better Display," p. 85)*.

The reason for all this activity is straightforward: the more they are studied, the more organic light-emitting diodes look to be just about everything their liquid-crystal counterparts are not. For starters, their structure is about as simple as one could imagine: an electrode, some organic stuff, then another electrode. Hook it up to a voltage and, presto, out comes light. There's no backlight, no diffuser, no polarizers or any of the other baggage that goes with liquid crystals *(see infographic below)*.

Such simplicity should translate into a manufacturing process between 20 and 50 percent cheaper than liquid crystal display processes. It also means a thinner and lighter screen with far lower power consumption: backlights in conventional screens are a major drain on laptop batteries. In addition, organic light-emitting diodes shine much brighter than their conventional rivals and are visible even in daylight. In short, enthuses analyst Mentley, "They have all the ideal features you look for in a display."

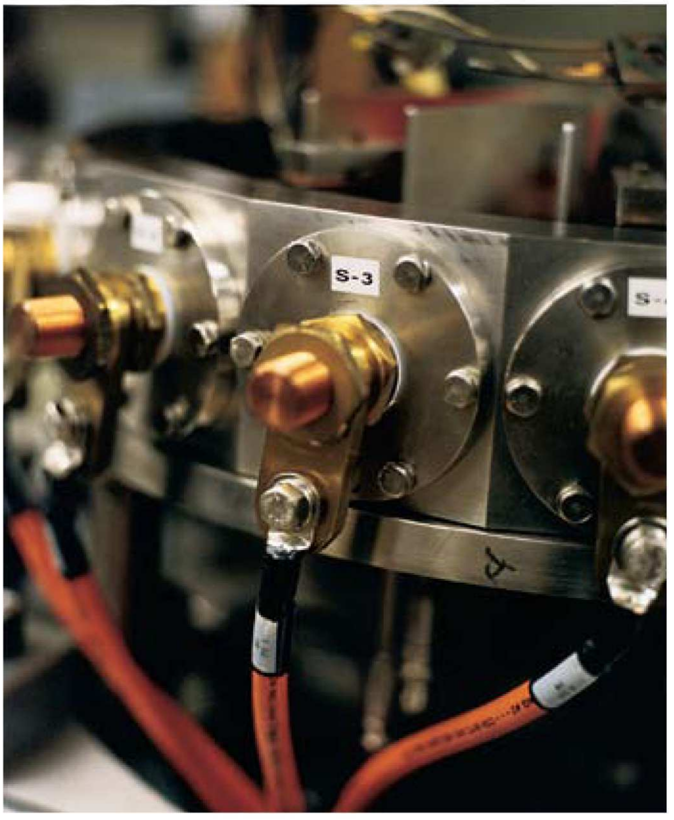
These impressive qualities have sparked a flood of gushy predictions about potential applications for organic light-emitting diodes that range from a

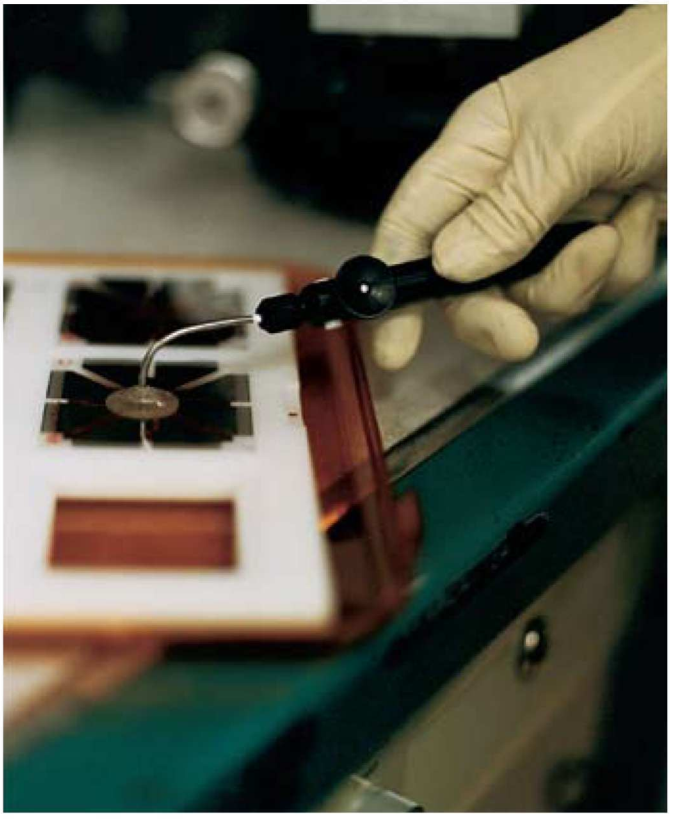
Cleaner Design, Brighter Image



No baggage: An active-matrix, color organic light-emitting diode (right) can be viewed as a streamlined version of a liquid crystal display (left). The basic structure: thin organic light emitters sandwiched between a cathode and a glass anode. Gone are the bulky diffuser, polarizers, and one of the glass substrates.

SLIM FILMS





Cooking up a feast for the eyes: At Kodak, a vacuum "coater" (left), where light-emitting organic materials are turned into the ultrathin films used in displays. A researcher wields a pickup tool (right) to load a glass substrate used in device fabrication into the coater.

new generation of affordable wall-hung TVs to highly flexible displays that can be rolled up and carried around like newspapers. It's still too early to evaluate most of these uses, which hinge on clearing formidable engineering hurdles. But there is one arena where the technology is ready to have immediate impact: cell phones.

On May 1, Japanese telecom giant NTT DoCoMo will launch the world's first third-generation mobile phone service. Organic light-emitting diodes represent the only display technology poised to meet all the requirements of the new standard, and the prize for winning the market will be significant. Overall sales of organic light-emitting diodes should grow from $3 million in 1999 to $2.7 billion in 2005, as they capture as much as 40 percent of the third-generation market, according to DisplaySearch, a consulting group based in Austin, TX. Even that figure may be conservative. "This is just a vast business, and there is an appetite for a better display," asserts Richard Friend of the University of Cambridge. In the third-generation marketplace, he predicts, the display will become the key differentiator between products.

The first phone to hit the market with an organic light-emitting diode display is Motorola's $300 Timeport P8767, which went on sale last September. Manufactured by Pioneer of Japan and based on small-molecule technology licensed from Kodak, it has a passive matrix display that is somewhat limited in its ability to show colors. Still, when stacked up against an equivalent LCD phone—the $250 Motorola P8167—its brightness and clarity are startling, and perhaps enough to justify the higher price tag. "There's no comparison as to which one people would rather have," claims Daniel Gisser, director of strategic marketing for Kodak's display business unit. "The OLED [organic light-emitting diode] looks so much better."

> "It's paper thin and really beautiful. They put it next to an active-matrix liquid crystal display, and it just blew the LCD away."

These are some of the first shots in the battle to dominate the third-generation market. More firepower is on the way. Last July, Seiko Epson demonstrated a cell phone-sized passive matrix screen—this time using polymer technology licensed from Cambridge Display Technology—capable of handling full-color video; production is scheduled to begin in mid-2002. Later this year, Samsung NEC Mobile Display, a joint venture formed last December, expects to begin producing 700,000 full-color, five-centimeter passive-matrix organic light-emitting diode displays a month.

INTO THE RED/GREEN/BLUE YONDER

All this activity represents the first wave of what many insiders believe will be a revolution in displays for devices ranging from small-screen applications such as digital camera viewfinders to handheld computers and laptops. Here, the stakes are far bigger than with cell phones, which DisplaySearch estimates will represent only about a tenth of the total $75 billion liquid crystal display market in 2005.

Last December, eMagin, a startup in Hopewell Junction, NY, made a first strike on this vast market by garnering the Society for Information Display's Dis-

play of the Year Gold Award for its advances in organic light-emitting diode technology, including a prototype 1.5-centimeter active matrix display it hopes will set a new standard for viewfinders. Then there's the hit of the prototypes, the Kodak-Sanyo 14-centimeter active matrix panel exhibited in Long Beach as the future of handheld devices like the Palm Pilot. "It's an absolutely fantastic-looking display," enthuses Nick Colaneri, director of new technology at Uniax, DuPont's just-acquired organic light-emitting diode subsidiary, which has its own offering in the works. "Paper thin, really beautiful. They put it next to an active matrix LCD, and it just blew the LCD away."

Indeed, if the industry buzz is to be believed, organic light-emitting diodes hold the potential to blow away the entire economics of display making. One approach is to dramatically lower manufacturing costs by printing displays directly from an inkjet printer onto a substrate. Last July, Seiko Epson demonstrated a full-color 6.3-centimeter screen made using this method. A next step might be to replace glass with plastic as the screen's substrate. That will produce a display cheaper, lighter and more rugged than today's organic offerings. But the critical point is that once the substrate is plastic, it is easy to imagine a transition from the current, hands-on batch production to an automated rolling process where displays are churned out more like newspapers than chips.

Beyond new forms of manufacturing comes a potentially even bigger step, in which polymers replace silicon in the thin-film transistors that form the active matrix backbone. Philips Electronics, Lucent Technologies, and Plastic Logic, formed last year by Richard Friend, are among those exhibiting prototype polymer transistors. Combined with a plastic substrate, this advance could enable a further milestone: electronic paper *(see "Electronic Paper Turns the Page,"* TR *March 2001)*.

Of course, talk about e-paper and other advanced applications is getting ahead of the story, since organic light-emitting diodes face obstacles in nearly every application. One serious current problem is color. Leave the Kodak screens on for a month or so, and the color becomes very nonuniform. Reds and blues die first, leaving a very green display. Cambridge Display Technology has done better with its polymer displays, achieving a working life of 100,000 hours for red and 30,000 hours for green—but just 1,000 hours for blue.

Both technologies are probably good enough for cell phones, which are typically used 200 hours a year and would likely be replaced before the colors start to fade. But such performance is not adequate for handheld or laptop displays, for which several thousand hours of life are required. "Whether the material technology can make it to that level has yet to be proven," admits Kodak's Tang. And the list of technical obstacles grows longer the farther out one looks.

Ultimately, however, the biggest challenge that organic light-emitting diodes face may not be so much technological as commercial. That is, while liquid crystal displays will probably fail to match the attractiveness or performance of organic light-emitting diodes, they will continue to be reliable and affordable—and their manufacturers will no doubt find ingenious ways of further lowering costs and improving capabilities. As analyst Mentley warns, "I haven't heard of any of these LCD guys saying they're just going to fold up and go away. It's going to be a battle."

Still, the battle is joined. And, as Richard Friend notes, few technologies last forever. "I mean, really new things will happen," he asserts. It looks as though organic displays could be one of those really startling new things that come barreling over the technology horizon. ◊

Global Race for a Better Display

Although organic light-emitting diode technology originated in the United States and Britain, firms around the globe are hot on the trail of commercial applications. Following are some of the most prominent players.

SMALL-MOLECULE DISPLAYS

Kodak began licensing passive matrix versions of its organic light-emitting diode technology in 1995. Long-standing licensees include TDK, Nippon Seiki and Pioneer, which has already commercialized the technology for use in car stereo displays and as an option on Motorola's Timeport cell phones. A recent licensee is Lite Array, a California startup with a production base in China.

Last October, Kodak set up its own business unit to pursue active matrix displays, establishing a partnership with Sanyo, a leader in the polysilicon transistors that might form the screens' backplanes. Polysilicon is faster than conventional amorphous-silicon thin-film transistors and therefore a potentially better match for organic light-emitting diode displays. Kodak has also licensed its technology to eMagin, a Hopewell Junction, NY, startup pursuing active matrix microdisplays for near-eye applications such as camera viewfinders.

The Motorola Timeport

COURTESY OF MOTOROLA

POLYMER DISPLAYS

Cambridge Display Technology began licensing its polymer technology in 1997. Its closest relationship is with Seiko Epson, which runs a lab next door to CDT. But the first license went to Philips, a player in cathode-ray tubes, plasma panels, active matrix LCDs and other display technologies. Philips's first product will be a backlight for liquid crystal displays.

Philips is also collaborating with DuPont, which in March acquired Uniax, a Santa Barbara, CA, startup founded on polymer technology from Nobel Laureate Alan Heeger.

The first commercial polymer organic light-emitting diode display—an alphanumeric screen—was to be launched this spring by Taiwan's Delta Optoelectronics, which works under a CDT license and uses materials from Dow Chemical.

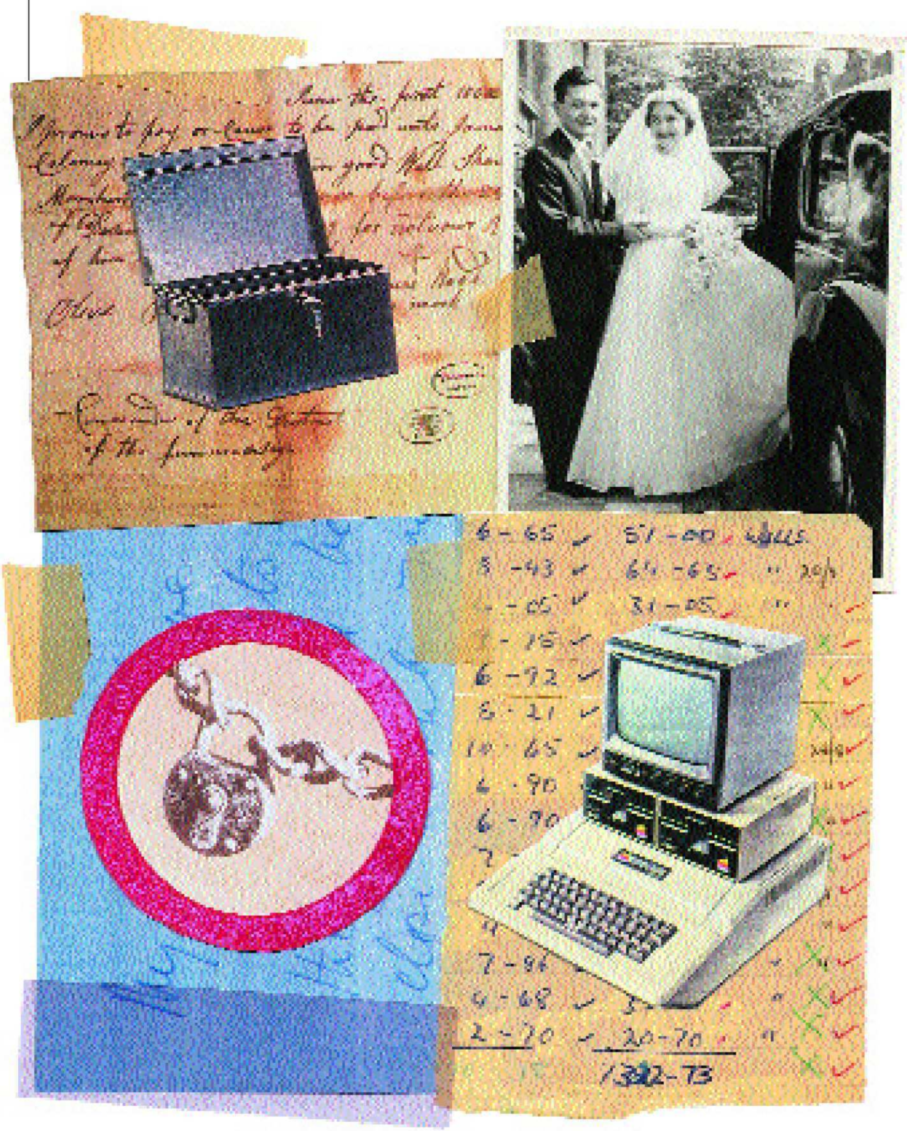
CDT's only other publicly announced agreements are with the German chemicals firm Hoechst and Agilent Technologies, a leader in inorganic light-emitting diodes.

Prominent independent makers of small-molecule organic light-emitting diodes include Samsung NEC Mobile Display and Princeton University spinoff Universal Display.

Remembrance of Things Past

I RECENTLY CLEANED OUT MY father-in-law's safe deposit box. There wasn't much in it: just a diamond ring that hadn't been worn in more than 30 years, and two birth certificates—one for him, and one for my recently deceased mother-in-law.

Years ago, a family's safe deposit box might hold a treasure trove of goods and documents. Opening a box, you might expect to find jewels, stock certificates, or the deed for some long-forgotten property. But that time is long past. These days, we use bits inside a computer's memory bank, not tokens of irreplaceable paper, to keep track of our life's records and our net worth. Few people hold stock certificates; information about stock ownership is kept in brokerage accounts. Few officials insist on seeing an original birth certificate; a fax or a photocopy will suffice. Even interest in gold and jewels seems to be faltering: in the 1960s, my father-in-law told me, his father gave him a gold watch—as something to sell if he were ever out of cash and needed to eat. Such was the mind-set of people who lived through the Great Depression. But these days, few people buy jewels for their investment potential. Instead, jewelry and gold is mostly bought for enjoyment and show.



MARTIN O'NEILL

Today it is data, more than money, that is the lifeblood of our society. And yet more than three decades into the "Information Age," data is something that we still don't quite understand how to steward. Data is not physical, not something that you can lock away today and hope you'll be able to access in 10 or 20 years. Large collections of data are almost impossible to safely maintain—especially over long periods. At the same time, data is just as difficult to dispose of properly. Indeed, individuals and businesses now have so much data in so many different formats on so many different computers that we are all heading for our own individual data catastrophes.

I once bought 10 used computers from a store that was going out of business. The machines were old and slow, but I didn't care—I wanted them for parts and software tinkering. I took them home, and just before I wiped their hard drives I decided to see what was on them.

I couldn't believe what I had stumbled upon. One computer had been a file server for a medium-sized law firm; with a few keystrokes I retrieved from its hard drive letters to clients, court filings and employee records. Another machine had been used by an organization that was delivering mental health services, and a third by a stockbroker: it had records of trades and account numbers, and more. Were I less scrupulous, I suppose that I could have had a lot of fun—and perhaps caused a lot of mischief—with the information that I had unwittingly purchased.

It's easy to chide the now-defunct store for failing to protect its customers, but the sad truth is that removing sensitive information from modern

computer systems is hard to do. As Oliver North learned during the Iran-Contra hearings, hitting "delete" is not enough. Instead, to properly clean, or "sanitize," a hard disk, it is necessary to overwrite every single block of storage. This can take hours, and even then it doesn't guarantee true erasure; readily available software tools can recover information after a disk has been "formatted." Most people don't bother sanitizing their computers before they throw them away: they just toss and pray.

Data is now our lifeblood. Yet as we store information in many different formats on many different computers, we are heading for our own individual data catastrophes.

My story isn't unique. Over the years there have been news reports of used computers turning up with records from the federal witness-protection program, pharmacies and police departments. And it's likely to be a growing problem: according to a 1997 study by researchers at Carnegie Mellon University, some 325 million computers will be obsolete by the year 2005. And that means a lot of potentially damaging information on the loose.

But at the same time that we are doing a poor job disposing of our data, we are doing an equally poor job of holding onto it.

In my basement, for instance, I have a collection of eight-inch floppy disks. These disks hold all of the papers and letters that I wrote in high school on the first computer that I ever owned. Alas, that machine has long since departed from the face of this planet. I doubt that I will ever be able to read those disks again, and I don't have a copy of the documents anywhere else.

The MIT Artificial Intelligence Laboratory had the same problem with a large collection of magnetic tapes made in the 1970s and '80s. Even the National Archives has had problems with computer records: you can't just leave them in a box. Instead, you need to copy them every three or four years from older computers to newer computers. Failure to do so risks losing the data as the magnetic medium deteriorates.

This endless cycle of copying is the approach that I now take with my home computer. On my computer there are three electronic folders that contain all the digital data from the last two decades of my life that I truly care about. There are three gigabytes of e-mail stretching back to 1983, another gigabyte of articles, letters and papers that I've written, and one more gigabyte of programs that I've coded, photographs I've taken, financial records and electronic keepsakes. Every time I get a new computer, I painstakingly copy this data from one machine to the next.

Organizing this data store over the past two decades has been a major challenge. But even after I got all of my directories set up, a continuing problem was software churn. For example, today's Microsoft Word can't read the letters that I wrote on my Macintosh in 1994 with WriteNow. Similarly, today's e-mail programs can't access the mailboxes of my old e-mail files, even though the messages themselves are stored as pure text. As a result, on those occasions that I need to go back and search for things, I usually end up using Unix and Linux tools that are comfortable working with pure text files, rather than the fancy Windows-based applications that can't handle even minor variations in file formats.

Another fear of mine is losing the data due to some sort of hardware failure. Like most computer users, I don't do a particularly good job of backing up. In all of last year, I made but a single tape backup. Instead, I protect my data by using multiple hard disks. The computer is set up so that every piece of information is recorded simultaneously onto two matched hard drives; if one drive fails, I still have a copy. As a second level of backup, at the end of each day my computer automatically copies the files that I've modified since the beginning of the month to a third hard drive. This archive has saved me on numerous times when I have accidentally deleted an important file. Even with these safeguards in place, though, I still manage to lose information from time to time.

All of this is a lot of work, but that's the price I pay to make sure my data is safe. Unfortunately, as hard disks have become more and more reliable, many people and organizations have forgotten the need to constantly back them up. In the old days, when hard drives might be expected to fail about once a year, you had a clear incentive to do your backups. Now that disks fail only every five or 10 years, keeping up sound data practices seems like busywork.

A growing number of companies are now trying to help businesses and individuals deal with these data issues. Retro Box, based in Columbus, OH, picks up a company's aging computers, properly sanitizes the hard drives and then helps to redeploy the computers within the corporation, sell them on the open market or donate them to charity. Several online backup companies, such as SkyDesk (www.backup.com) and Connected (www.connected.com), will back up your files over the Internet to their own data vaults. Of course, if you actually use one of these companies, you need to trust them more than you trust yourself.

I'm sure that over the next 20 or 30 years we'll finally get the hang of this data thing. Years from now, when my grandchildren go to clean out my safe deposit box, they'll probably sit down at a computer terminal somewhere, have their eyes scanned by some kind of biometric reader and transfer the data from my data vault to theirs. Either that, or they'll just hit "delete" and wipe it all away. ◊

MP3 Software

The controversial program removes superfluous data from digital sound files.

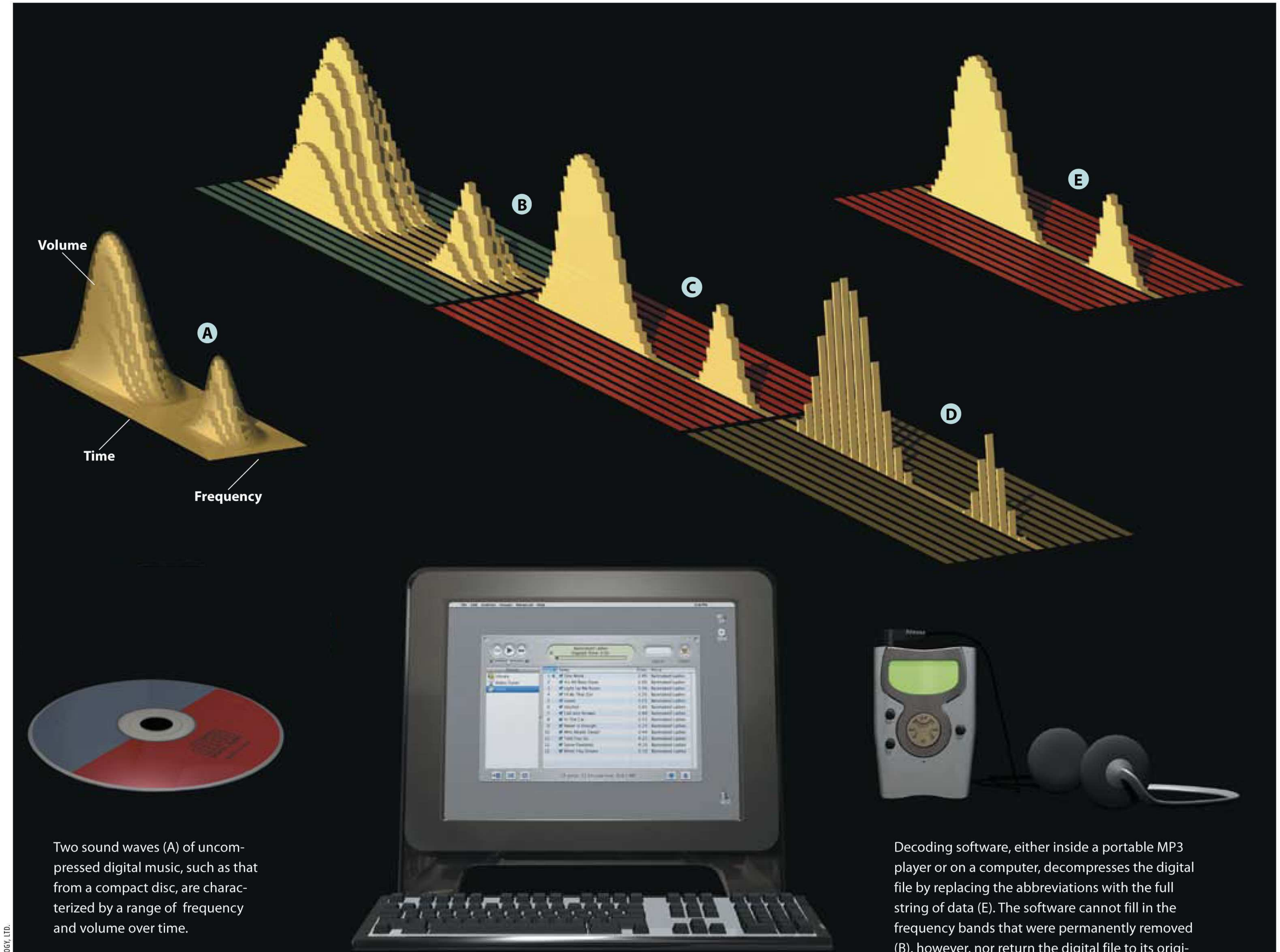
A funny thing happens when we listen to music. We don't hear it all. Of the complex acoustical mix that seduces our ears when a song plays, we're capable of discerning only the most dominant qualities. If two similar frequencies are playing at the same time, for example, we detect the louder one; if a soft sound follows a louder one, it can take up to a tenth of a second for us to hear the subtler tone.

MP3 technology takes advantage of our auditory shortcomings to shrink digital music files by a factor of 10 or more without sacrificing the quality of the listening experience. The software eliminates what our ears can't discern, then replaces redundancies in the remaining string of digital bits with abbreviations. MP3 can turn a 50-megabyte file that would otherwise take hours to download from the Internet into a five-megabyte file that takes minutes. Consequently, consumers have access to high-quality music recordings on Web sites such as Napster and MP3.com—a threat to CD sales that currently has the recording industry in a snit.

Although the MP3 hullabaloo is fairly recent, the technology has been around since the Erlangen, Germany, research facility the Fraunhofer Institute for Integrated Circuits acquired a German patent for it in 1989. (The U.S. patent was approved in 1996.) Fraunhofer allowed free use of the technology in its early days, giving developers a chance to improve its encoding and decoding performance. It was soon integrated into the Moving Picture Experts Group's standards for the compression of digitized audio and video. (The name MP3 itself comes from the group's acronym, MPEG, and stands for MPEG audio, layer three.) The first MP3-playing software, the Amp, was created in 1997 by Advanced Multimedia Products and became a model for later Windows- and Mac-based devices such as WinAmp and MacAmp.

In September 1998, the Fraunhofer Institute announced that it would begin collecting royalties and charging developers a license fee of $15,000 annually. The threat of fines or suit has had little apparent impact on the MP3 movement. Today, "MP3" is the second most popular search word on the Internet, behind "sex." ◊

ILLUSTRATION: JOHN MACNEILL; PHOTOGRAPH COURTESY OF CREATIVE TECHNOLOGY, LTD.



Two sound waves (A) of uncompressed digital music, such as that from a compact disc, are characterized by a range of frequency and volume over time.

Once the song is copied to the computer, MP3 software compresses the signal by removing the sound elements we can't hear and then replacing redundancies with a kind of digital shorthand. It accomplishes this first by splitting the signal into frequency bands (B). The software then identifies and permanently removes frequencies our ears can't discern, leaving only what we can hear (C). Finally, it temporarily replaces highly repetitive strings of bits in the remaining signal with digital abbreviations that take up far less room (D).

Decoding software, either inside a portable MP3 player or on a computer, decompresses the digital file by replacing the abbreviations with the full string of data (E). The software cannot fill in the frequency bands that were permanently removed (B), however, nor return the digital file to its originally recorded format (A).

Information Cosmos

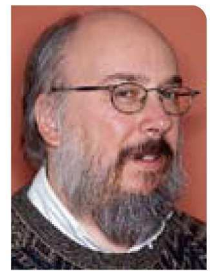
THE CLASSICAL WORLD OFFers a legendary story about enlightenment through assembled knowledge—the great Library at Alexandria—that embodies both our hopes and our anxieties for the digital age. Will innovation and free inquiry thrive amid the Web's great storehouses of knowledge? Or will an information elite monopolize access to knowledge and grow increasingly isolated from the public?

Later this year, a state-of-the-art research facility opens in Alexandria, transforming legend back into reality. Announcing the project, Egyptian first lady Suzanne Mubarak vowed the new Bibliotheca Alexandrina would be "a digital lighthouse for the world." Many countries are contributing precious archival holdings on microfilm or CD-ROM and returning documents confiscated during wars and occupations.

Alexander the Great conceived the original library as a tribute to his teacher, Aristotle. For over 600 years, it attracted the ancient world's greatest scholars. In its confines, Euclid mastered geometry, Archimedes struggled with mechanics, Ptolemy constructed his astronomical model, and Herophilus located intelligence within the brain. The library's destruction signaled the onset of the Dark Ages. The erection of the new facility invites us to consider the lessons its predecessor's history holds for the information age:

- **Information is not knowledge.** The Alexandrian librarians didn't just collect documents; they struggled to create order (cosmos) from chaos. They developed cataloguing systems, defined disciplines, and produced definitive editions of significant works. Today's interfaces and search engines must support multiple paths to knowledge, but our ultimate goal must still be to seek order from informational chaos.
- **Information is a global resource.** Alexander built his city at the crossroads of Europe, Africa and Asia. His empire was populated by people from across the world. He encouraged intermarriage and respect for all faiths. The library extended these ideals, preserving works from diverse traditions. Modern archives must do the same.
- **Theory must be grounded.** Alongside the reading rooms stood a menagerie, an observatory, a dissecting room, botanical gardens and a cafeteria where scholars broke bread together. Their work combined making and thinking, the sciences and the humanities, the stench of pachyderms and the crackle of papyrus. Insofar as contemporary education encourages abstraction over experience and specialization over breadth, it compromises those ideals.
- **Power corrupts.** In his desire to amass knowledge, Alexander granted librarians almost unlimited power. Ships entering the port were raided, all books confiscated. The owners later received copies; the originals remained state property. However worthy its aims, state power represents a danger to liberty and must be carefully monitored.
- **Ignorance breeds backlash.** While a resource for scholars, the library remained closed to the public. Demagogues exploited that isolation, stirring up the masses. The resulting culture war pitted Christians against "pagans," the public against scholars. Rioters seized Hypathia, a remarkable woman who had made major contributions to math, physics and astronomy, dragging her from her chariot and slashing her with seashells. Mobs reportedly looted and destroyed the library itself. In the absence of public discussion, ignorance begets moral panic.
- **Centralization represents vulnerability, not strength.** The librarian's dream was to assemble all the world's books in one location. Ptolemy III, for example, coveted the original manuscripts of Sophocles, Aeschylus and Euripides. When the Athenians refused to part with them, Ptolemy left a deposit in gold for their loan. Then, he forfeited the treasure, keeping the manuscripts, which perished with the library. How many more masterworks might have survived if they had remained in Athens? The strength of the new digital culture is that it originates from many sources, is stored on many servers and is distributed through a variety of pathways. We should be leery of schemes that compromise these systems.

Egypt's first lady vows that Alexandria's new library will be "a digital lighthouse." But the information age can still learn from the facility's ancient predecessor.



Planners of the Bibliotheca Alexandrina seem to have learned many of these lessons. The extraordinary facility will have reading rooms larger than Grand Central Station, architecture that fuses ancient symbols with futuristic structures, and a computer catalogue that enables searches in multiple languages. It will also incorporate a planetarium, an Information Studies school, and museums of archaeology, calligraphy and science. Its stacks will be open to scholars and the general public. The modest initial collection of 300,000 books falls short of amassing all the world's knowledge, but the library's real importance is symbolic, enabling Egypt to embrace its cosmopolitan past and holding open the ideal of intellectual freedom against a sometimes repressive government. Still, I wonder if Egypt—and the modern world in general—is ready to revive the ideals of the ancient library. Or is the facility's mission doomed to be compromised by social and political forces beyond its control? ◊

ESSAY | BY ANDREW ODLYZKO

The Myth of "Internet Time"

Technological changes take years to diffuse through the economy. Contrary to popular wisdom, the Internet is no exception.

With the bursting of the high-tech bubble, the prevailing social mood is shifting from Internet worship to cynicism. The attitude that "the Internet changes everything" has given way in some quarters to denigration of the Net as a fad—the citizen's band radio of the 1990s. Yet just as the early tone was overoptimistic, the new one could easily become unjustifiably pessimistic. To avoid overreactions, it might be useful to analyze what propelled the dot-com craze to the ridiculous heights it reached in 1999 and early 2000.

That this was a craze is becoming ever clearer. In the spring of 1999, for example, Silicon Valley venture capitalists vied for the privilege of funding more than half a dozen companies operating Web-based portals for pet-related products, services and information. In retrospect, it is clear that not even one of those companies could have been successful. Yet somehow all those venture capitalists, as well as the staffs of the startups, went along for the wild ride. The press and the general public also willingly and enthusiastically joined in the celebration of what promised to be a brave new world, where conventional business principles no longer applied.

Why were they all so wrong?

A few key interrelated and mutually reinforcing ideas appear to have led even the most experienced people astray. The most important was that of "Internet time." This was the perception that product development and consumer acceptance were now occurring in a fraction of the time that they traditionally took. Closely related to the concept of Internet time was the idea that the first company to establish itself in a new market would have an almost unassailable advantage over latecomers—the so-called first-mover advantage. Further support for the dot-com craze was provided by the notion of "network effects," in which consumers and producers adopting a new product or service would induce others to do the same.

Network effects are real enough, and they are much more important on the Internet than in the traditional economy—although probably not as important as their main proponents argue, nor as easy to practice. But it is the idea of Internet time that was the most fundamental. If indeed product cycles were now compressed from the traditional seven years down to one year, then anything might change in the blink of an eye. Internet time appeared to give special power to the first-mover advantage. A company that could quickly establish itself as a pets portal, for example, might be able to gain a high enough market share to discourage competition. The world would fall into utter dependence on the startup for anything remotely related to pets. In that environment, any notion of due

JANA LEON

diligence gave ground to the overwhelming compulsion to be a part of the new gold rush.

The fatal defect of this line of reasoning is that it is based on myths. As with all myths, they do have some evidence supporting them. For example, Yahoo!, the first portal company, has managed to maintain its preeminence. Amazon.com has also remained the dominant online retailer for many years (although whether it can ever be profitable is increasingly in doubt). However, being first—or even one of the first—doesn't necessarily confer an overwhelming advantage. Just consider the early personal computer pioneers, such as Atari. Where are they now? Even the recent history of the Internet abounds in counterexamples to the thesis of first-mover advantage. Look at the market for Internet search engines. Five years ago, AltaVista achieved a technical breakthrough that propelled it to dominant status on the world's desktops. Today, AltaVista is a distant also-ran.

The main reason the first-mover advantage is much less potent than is commonly claimed is that Internet time, the dominant theme of the dot-com bubble, is false. Yes, product development cycles have become noticeably shorter. This is true not just in software, but also in such old-economy products as cars. But consumers do not operate on Internet time. Novel technologies do not diffuse notably more rapidly than they did in the days before dot coms strode the earth.

The thesis of Internet time rests largely on a misreading of transient phenomena. One often-recited factoid, for example, has it that Internet traffic has been doubling every three months, which corresponds to an astronomically high annual growth rate of about 1,500 percent. In truth, however, Net traffic grew at that torrid pace for one brief period during 1995-96. Since then, annual growth in traffic has been in the neighborhood of 100 percent—still an impressive statistic, but not nearly as earth-shattering as the myth would have us believe.

Another principal piece of evidence for a speeded-up world is the rapid adoption by the masses of a strikingly new product: the Web browser. The first beta version of Mosaic was released in early 1993, and by the end of 1994 Web traffic dominated the Internet, as millions of people rushed online. However, that is looking very much like an extreme exception. It has taken about six years for a new browser standard (called HTTP/1.1) to finally creep toward dominance. And IPv6, an Internet protocol designed to solve nagging technical problems such as the limited number of available addresses, is still used on only a small scale. It, too, was introduced in the mid-1990s. And even though Amazon.com is the dominant online bookseller, after nearly six years in business the company accounts for less than 10 percent of U.S. book sales. While 10 percent would be an impressively high market share by conventional standards, it doesn't match the predictions that online retailers would wipe out the low-tech competition.

These examples are not aberrations. In 1995, technology sages were predicting that Internet telephony meant imminent doom to the established phone companies. But today, while it is possible to place voice calls through the Net, only a small (though rapidly growing) number of people do it. Similarly, eBay, for all its successes as a Web auction site, has so far had little impact on the classified ads that sustain newspapers. Make no mistake, all these technologies and companies are transforming the economy. They're just not doing it in Internet time.

As a general historical rule, it takes about a decade for even the most compelling new product or service to be widely accepted. That's still true. Even such attractive technologies as music CDs and cell phones, which many of us now regard as indispensable, took more than 10 years to move from commercial introduction to widespread use. Today we are seeing similar rates of adoption for DVDs, as well as digital cable TV, personal digital assistants and other emerging technologies.

THE THESIS OF "INTERNET TIME" RESTS LARGELY ON A MISREADING OF TRANSIENT PHENOMENA, SUCH AS THE TORRID GROWTH OF NET TRAFFIC IN 1995-96.

At this stage, some readers might ask about Napster, the popular (and controversial) service for swapping digitized music files over the Net. Isn't this an example of a technology rivaling the Web browser in its rate of diffusion? The answer is: probably not. Yes, Napster did spread extremely rapidly among college students. Within a year and a half of its release, it accounted for about a quarter of Internet traffic at several universities. On a wider scale, however, Napster's impact has been muted. It is a threat to the music industry, but it has not driven it into the ground. Indeed, sales of recorded music in 2000 set records.

The slow diffusion of novel technologies explains the ability of traditional businesses to resist the onslaught of the startups. Since their customers were not changing on Internet time, the brick-and-mortar enterprises had time to adapt. This is similar to what has happened in the past. When the telegraph and then the telephone arrived, we didn't get "t-businesses." When power generators first made electricity readily available, we didn't get an early form of "e-businesses." What we got were two types of businesses. There were those that reshaped themselves to use the telegraph, the telephone and electricity. And then there were the dead ones, which refused to adapt.

The Internet is a potent communication tool, offering unprecedented speed and reach. It does change everything, just as the telegraph, the telephone and electricity eventually did. It is just that people do not operate on Internet time—and therefore the truly large implications of this new technology are likely to take many decades to unfold. ◊

Andrew Odlyzko is head of mathematics and cryptography research at AT&T Labs in Florham Park, NJ, and a frequent commentator on Internet trends.

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People and Organizations Mentioned in This Issue

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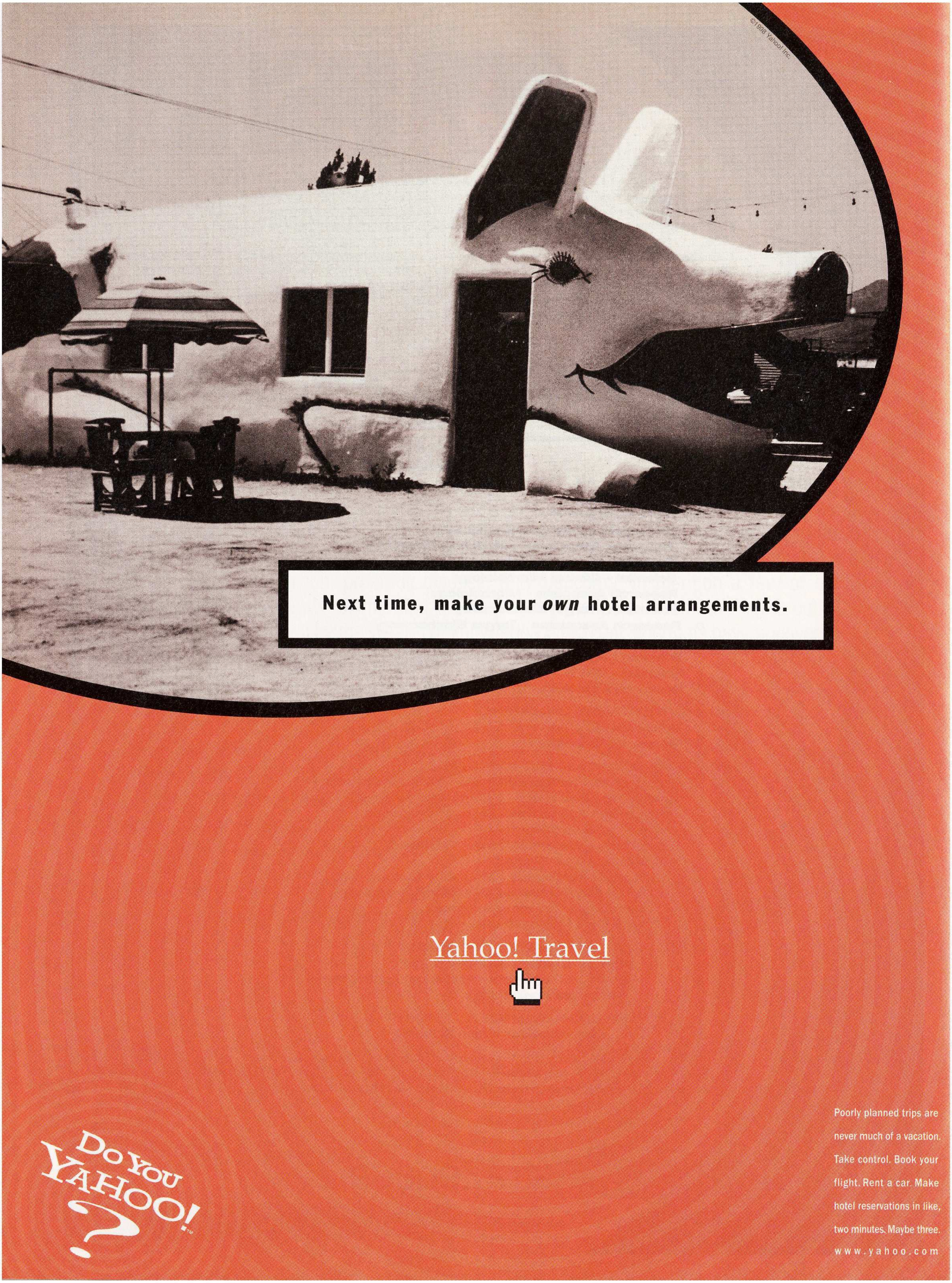
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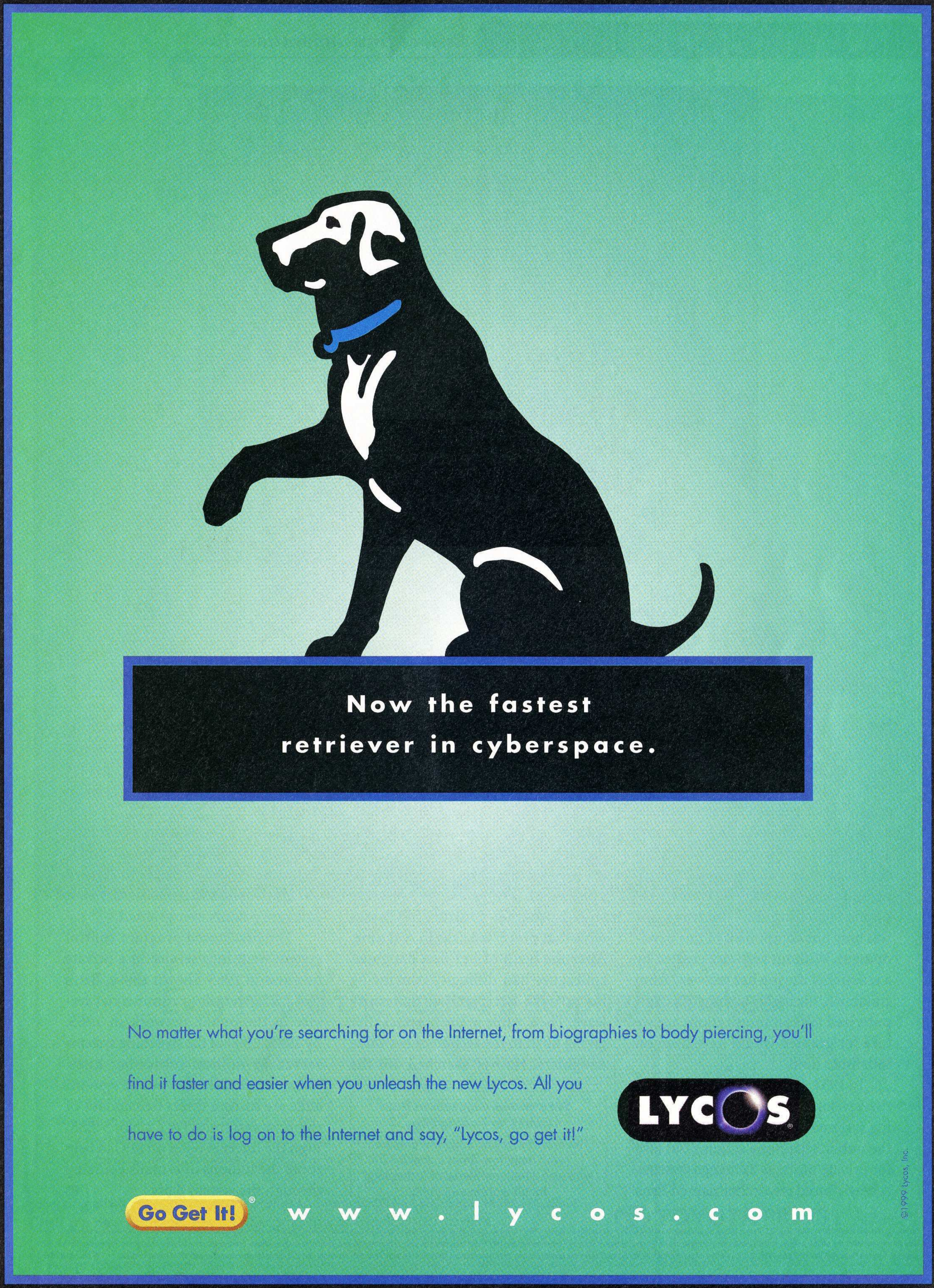
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COURTESY OF AT&T

Software Switch

Erna Hoover delivered the idea that saved us from jammed switchboards

IN 1947, BELL LABS LAUNCHED a revolution with the introduction of the transistor, enabling everything from radios to computers to be made smaller and more cheaply. The transistor also made possible a less visible technology, one that allowed telecommunications to explode: electronic telephone switching. But the transistor was only one component of this development. Without software created by a researcher during her recovery from childbirth, the highly automated, computerized telecommunications age we take for granted would have been on indefinite hold.

In 1952, Bell Labs began exploring the development of electronic switching systems (ESS) for use not only by the public telephone systems but also for private business exchange systems. A newly hired researcher named Erna Schneider Hoover joined the team in 1954. Hoover was not a typical team member: not only was she female, but she came to Bell Labs with a degree in medieval history from Wellesley College and a doctorate in logic and philosophy of science from Yale.

Hoover contributed to the development of innovative software for stored program control (SPC) systems that processed calls in real time. After the birth of her first daughter, colleagues had difficulty convincing her to take her planned maternity leave. Then, while in the hospital after giving birth to the second of her three daughters, Hoover sketched out the first plans for a program to monitor the frequency of incoming calls and automatically adjust the acceptance rate, eliminating the danger of system overloads.

Hoover's innovation eventually earned her a position as the first female department head at Bell Labs. And in 1971, it earned her one of the first software patents ever granted.

The first stored program control system went into service in a private business in 1963. Shown above, Bell's No. 1 ESS went into commercial service in the public network in 1965. By 1983, 1,800 of the switching systems served 53 million subscriber lines. Today, businesses and public systems alike are using a direct descendant of the first system: AT&T's No. 5 ESS. Even the Internet relies on SPC to help route the billions of e-mails coursing through the system daily. ◊

We welcome suggestions from readers for Trailing Edge.

This month's Trailing Edge was prepared with help from Amos E. Joel Jr., who won a National Medal of Technology for his work in switching.

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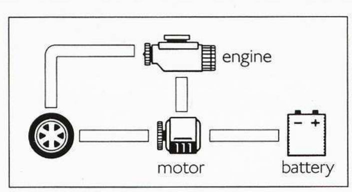

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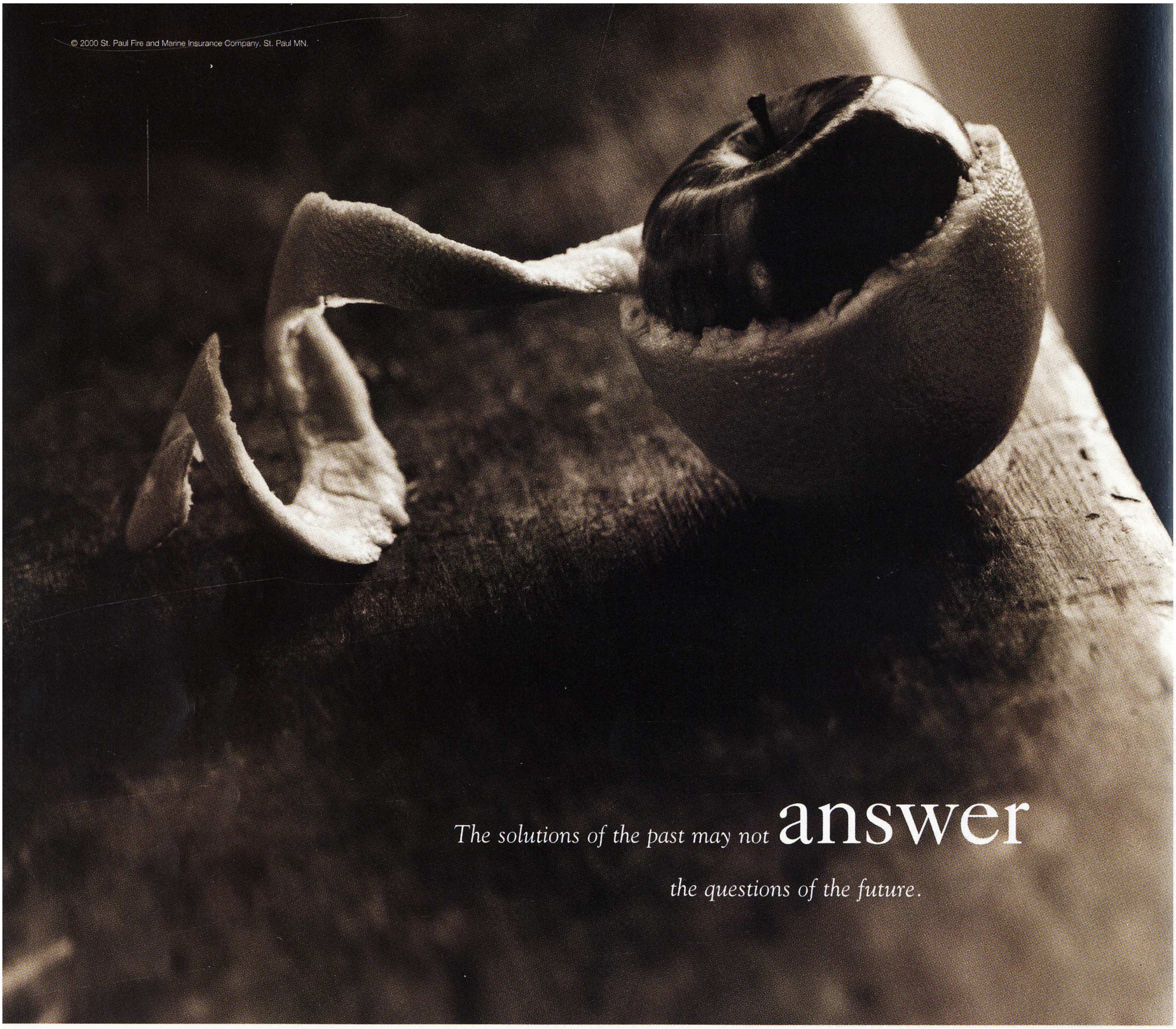
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